

10/772219

=> file registry

FILE 'REGISTRY' ENTERED AT 11:35:30 ON 20 AUG 2007

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STRUCTURE FILE UPDATES: 19 AUG 2007 HIGHEST RN 944998-48-5

DICTIONARY FILE UPDATES: 19 AUG 2007 HIGHEST RN 944998-48-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

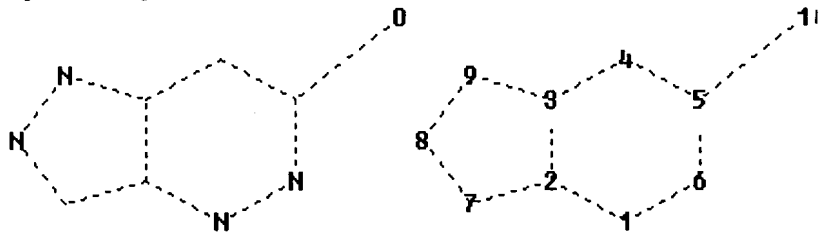
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

Uploading L3.str



chain nodes :

10

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

5-10

ring bonds :

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9

exact/norm bonds :

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 5-10 7-8 8-9

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

=> file zcaplus

FILE 'ZCAPLUS' ENTERED AT 11:35:35 ON 20 AUG 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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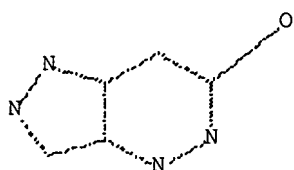
FILE COVERS 1907 - 20 Aug 2007 VOL 147 ISS 9  
FILE LAST UPDATED: 19 Aug 2007 (20070819/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L14  
L3 STR



Structure attributes must be viewed using STN Express query preparation.

L5	80	SEA	FILE=REGISTRY	SSS	FUL	L3	
L6	17	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L5	
L7	3886	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	GREEN J?/AU	
L8	285	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	GREY R?/AU	
L9	422	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	PIERCE A?/AU	
L10	2	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L7 AND L8 AND L9	
L11	6	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L7 AND (L8 OR L9)	
L12	4	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	L8 AND L9	
L13	4	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	(L7 OR L8 OR L9) AND L6	
L14	11	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	(L10 OR L11 OR L12 OR L13)	

=> file marpat

FILE 'MARPAT' ENTERED AT 11:35:50 ON 20 AUG 2007  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE CONTENT: 1961-PRESENT VOL 147 ISS 7 (20070817/ED)

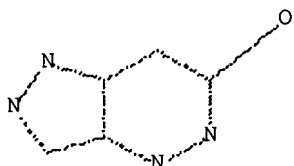
SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2007155779	05	JUL	2007
DE	102005063244	28	JUN	2007
EP	1801190	27	JUN	2007
JP	2007173472	05	JUL	2007
WO	2007076379	05	JUL	2007
GB	2433499	27	JUN	2007
FR	2895408	29	JUN	2007
RU	2302407	10	JUL	2007
CA	2571093	16	JUN	2007

Expanded G-group definition display now available.

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L3 STR



Structure attributes must be viewed using STN Express query preparation.

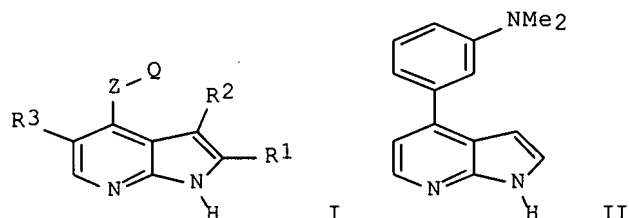
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L8	285	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	GREY R?/AU
L9	422	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	PIERCE A?/AU
L25	31	SEA	FILE=MARPAT	SSS	FUL	L3
L29	28	SEA	FILE=MARPAT	ABB=ON	PLU=ON	L25 NOT (L7 OR L8 OR L9)
L30	3	SEA	FILE=MARPAT	ABB=ON	PLU=ON	L25 NOT L29

=> d ibib abs hitstr L14 1-11; d ibib abs qhit L30 1-3  
YOU HAVE REQUESTED DATA FROM FILE 'ZCAPLUS' - CONTINUE? (Y)/N:y

L14 ANSWER 1 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2006:1252802 ZCAPLUS Full-text  
DOCUMENT NUMBER: 146:27814  
TITLE: Pyrrolopyridines useful as inhibitors of protein kinase and their preparation, pharmaceutical compositions, and use in the treatment of various diseases  
INVENTOR(S): Ledebor, Mark W.; Wannamaker, Marion W.; Farmer, Luc J.; Wang, Tiansheng; **Pierce, Albert C.**; Martinez-Botella, Gabriel; Bethiel, Randy S.; Bemis, Guy W.; Wang, Jian; Salituro, Francesco G.; Arnost, Michael J.; Come, Jon H.; **Green, Jeremy**; Stewart, Michelle; Marhefka, Craig  
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
SOURCE: PCT Int. Appl., 201pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006127587	A1	20061130	WO 2006-US19711	20060522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007135466	A1	20070614	US 2006-438748	20060522
PRIORITY APPLN. INFO.:			US 2005-683554P	P 20050520
OTHER SOURCE(S):			MARPAT 146:27814	
GI				



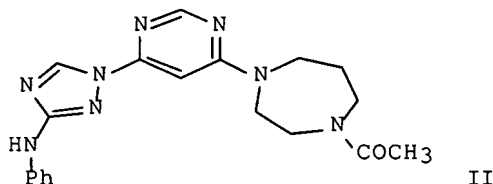
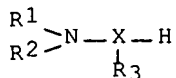
AB The invention relates to compds. of formula I, which are useful as inhibitors of protein kinases, particularly of JAK family and ROCK family kinases. The invention also provides pharmaceutically acceptable compns. comprising said compds. and methods of using the compns. in the treatment of various disease, conditions, or disorders. Compds. of formula I wherein Q is a (un)substituted (un)saturated 3- to 8-membered (hetero)monocyclic ring and (un)saturated 8- to 12-membered (hetero)bicyclic ring; Z is a bond, NH, Cl-3 alkylamine, and C=CH<sub>2</sub>; R1 and R2 are independently (un)substituted Cl-2 alkyl; R3 is H, Cn, NO<sub>2</sub>, (un)substituted Cl-6 aliphatic; and their pharmaceutically acceptable salts thereof are claimed. Example compound II was prepared by cross-coupling of 4-bromo-1-tosyl-1H-[2,3-b]pyridine with 3-dimethylaminophenylboronic acid derivative. All the invention compds. were evaluated for their JAK and ROCK kinase inhibitory activity. From the kinase inhibition assay, it was determined that compound II exhibited Ki values of less than 0.5  $\mu$ M against JAK2, JAK3 and ROCK-I.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2005:136554 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 142:240435  
 TITLE: Preparation of aminotriazole compounds useful as

INVENTOR(S): inhibitors of protein kinases  
 Davies, Robert J.; Arnost, Michael J.; Bemis, Guy W.;  
 Forster, Cornelia J.; **Grey, Ronald, Jr.**;  
 Ledford, Brian; Marhefka, Craig; Messersmith, David;  
**Pierce, Albert C.**; Salituro, Francesco; Wang,  
 Jian  
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA; Ledebøer,  
 Mark W.  
 SOURCE: PCT Int. Appl., 190 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005013982	A1	20050217	WO 2004-US25539	20040806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004263148	A1	20050217	AU 2004-263148	20040806
CA 2534921	A1	20050217	CA 2004-2534921	20040806
US 2005261268	A1	20051124	US 2004-914051	20040806
US 7226920	B2	20070605		
EP 1663211	A1	20060607	EP 2004-780381	20040806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007501257	T	20070125	JP 2006-522766	20040806
PRIORITY APPLN. INFO.:			US 2003-492787P	P 20030806
			WO 2004-US25539	W 20040806
OTHER SOURCE(S):			CASREACT 142:240435; MARPAT 142:240435	
GI				



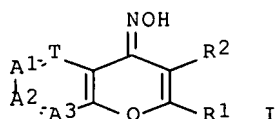
AB Title compds. I [X = 1,2,4-triazolyl; R<sub>1</sub> = H or alkyl; R<sub>2</sub> = alkyl, arylalkyl, heterocyclicalkyl, etc.; or R<sub>1</sub> and R<sub>2</sub> together with the N form an (un)substituted heterocyclyl or heteroaryl ring; R<sub>3</sub> = alkyl, arylalkyl, heterocyclicalkyl, etc.], and their pharmaceutically acceptable salts, are

prepared and disclosed as inhibitors of protein kinases. Thus, e.g., II, was prepared by substitution of 1-(6-chloropyrimidin-4-yl)-3-phenylamino-1H-[1,2,4]triazole (preparation given) with N-acetylhomopiperazine. I were tested vs. numerous kinases for their inhibitory activity, e.g., selected compds. of I possessed IC50 values of < than 0.1 µM against FLT-3. The invention also provides pharmaceutical compns. comprising the compds. of the invention, processes for preparing the compds. and methods of using the compns. in the treatment of various disorders.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2004:825133 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 141:332051  
 TITLE: Preparation of substituted chromen-4-one oximes as inhibitors of protein kinases  
 INVENTOR(S): **Green, Jeremy; Aronov, Alex; Pierce, Albert C.**  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 47 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2004198750	A1	20041007	US 2004-808678	20040325
AU 2004230841	A1	20041028	AU 2004-230841	20040325
CA 2522595	A1	20041028	CA 2004-2522595	20040325
WO 2004092154	A1	20041028	WO 2004-US9145	20040325
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1615906	A1	20060118	EP 2004-758959	20040325
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
JP 2006522124	T	20060928	JP 2006-509283	20040325
PRIORITY APPLN. INFO.:			US 2003-460042P	P 20030403
			WO 2004-US9145	W 20040325
OTHER SOURCE(S):			MARPAT 141:332051	
GI				



AB The title compds. [I; R1 = LmR, LmArl, LmCyl; L = S, O, NR, alkylidene wherein up to two non-adjacent methylene units of L are optionally replaced by S, O, CO, etc.; m = 0-1; Ar1 = (un)substituted 5-7 membered monocyclic or 8-10 membered bicyclic ring having 0-5 heteroatoms; Cyl = (un)substituted 3-7 membered (un)saturated monocyclic ring having 0-3 heteroatoms or 8-10 membered (un)saturated bicyclic ring having 0-5 heteroatoms; R = H, alkyl; R2 = H, CN, SR, OR, etc.; T = N, CR3; A1-A3 = N, CR4; provided that no more than two of T, A1-A3 are N atom; R3 = H, halo, NO2, etc.; R4 = halo, NO2, CN, etc.; with provisos], useful as inhibitors of protein kinases, were prepared E.g., a 2-step synthesis of 2-(4-methoxyphenyl)-8-methylchromen-4-one oxime, starting from 8-methyl-4'-methoxyflavone, was given. The exemplified compds. I were tested and found to inhibit CDK-2, cMET, GSK-3, SYK, ZAP-70, FLT-3, JAK-3, p70S6K, TAK-1, and IRAK-4. The invention also provides pharmaceutically acceptable compns. comprising said compds. I and methods of using the compns. in the treatment of various disease, conditions, or disorders.

L14 ANSWER 4 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:696343 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:225525

TITLE: Preparation of pyrazolopyridazines as inhibitors of protein kinases

INVENTOR(S): *Green, Jeremy; Grey, Ronald; Pierce, Albert C.*

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

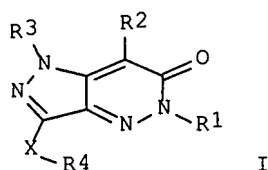
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072029	A2	20040826	WO 2004-US3061	20040204
WO 2004072029	A3	20041216		
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RW:	BW, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004192682	A1	20040930	US 2004-772219	20040204
PRIORITY APPLN. INFO.:			US 2003-445529P	P 20030206
			WO 2004-US3061	A 20040204
OTHER SOURCE(S):	MARPAT 141:225525			
GI				



AB The title compds. [I; R1 = substituted Ph, alkylphenyl, CH<sub>2</sub>Ph, etc.; R2 = halo, NO<sub>2</sub>, CN, etc.; R3 = H, alkyl; X = a bond, O, S, (un)unsubstituted NH; R4 = H, quinazolinyl, pyrimidinyl, etc.] which are inhibitors of protein kinases, particularly inhibitors of GSK mammalian protein kinase, and more particularly inhibitors of GSK-3 mammalian protein kinase, were prepared E.g., a multi-step synthesis of 3-amino-5-(3,4-dimethoxyphenyl)-1,5-dihydropyrazolo[4,3-c]pyridazine-6-one, starting from 3,4-dimethoxyaniline and di-Me acetonediacarboxylate, was given. The representative compds. I were shown to have K<sub>i</sub> of < 4.0 μM for GSK-3β. The invention also provides pharmaceutically acceptable compns. comprising the compds. I and methods of utilizing those compds. and compns. in the treatment of various protein kinase mediated disorders.

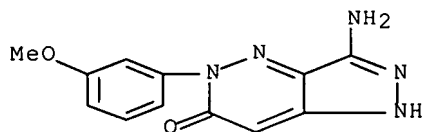
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 746647-47-2P 746647-48-3P 746647-49-4P  
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 746647-71-2P 746647-72-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyridazines as inhibitors of protein kinases)

RN 746647-38-1 ZCAPLUS

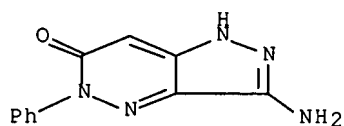
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 746647-39-2 ZCAPLUS

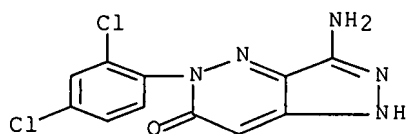
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-phenyl- (9CI) (CA INDEX NAME)





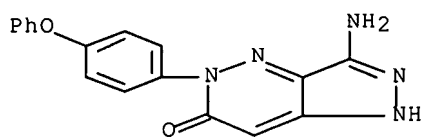
RN 746647-40-5 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-5-(2,4-dichlorophenyl)-1,5-dihydro- (9CI) (CA INDEX NAME)



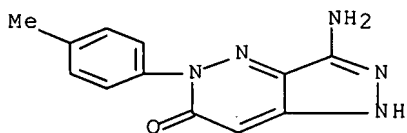
RN 746647-41-6 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



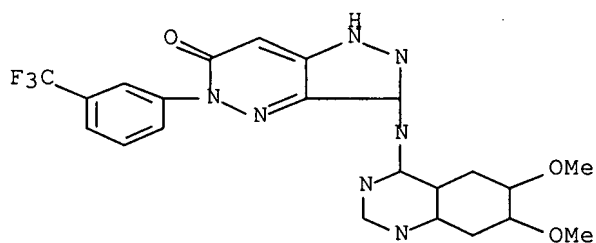
RN 746647-42-7 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 746647-43-8 ZCAPLUS

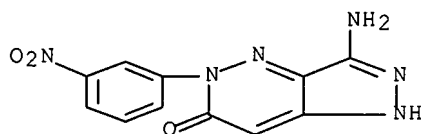
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-[(6,7-dimethoxy-4-quinazolinyl)amino]-1,5-dihydro-5-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

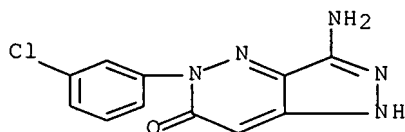
RN 746647-44-9 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(3-nitrophenyl)-  
(9CI) (CA INDEX NAME)



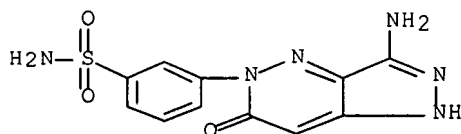
RN 746647-45-0 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-5-(3-chlorophenyl)-1,5-dihydro-  
(9CI) (CA INDEX NAME)



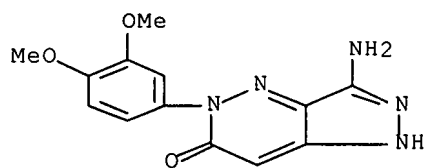
RN 746647-46-1 ZCAPLUS

CN Benzenesulfonamide, 3-(3-amino-1,6-dihydro-6-oxo-5H-pyrazolo[4,3-  
c]pyridazin-5-yl)- (9CI) (CA INDEX NAME)



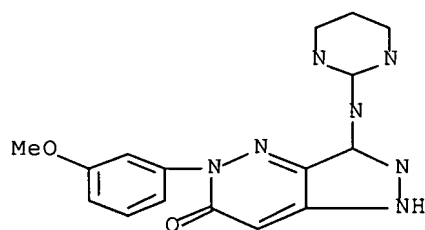
RN 746647-47-2 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-5-(3,4-dimethoxyphenyl)-1,5-  
dihydro- (9CI) (CA INDEX NAME)



RN 746647-48-3 ZCAPLUS

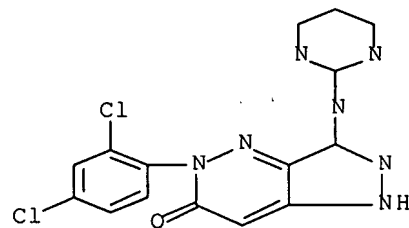
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-(2-pyrimidinylamino)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 746647-49-4 ZCAPLUS

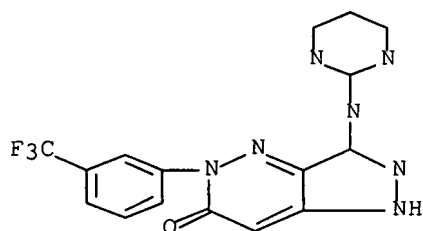
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-(2-pyrimidinylamino)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 746647-50-7 ZCAPLUS

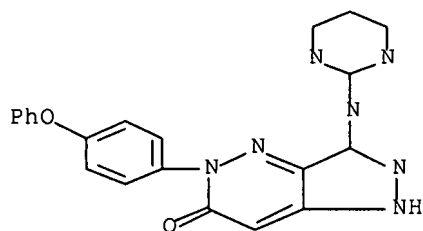
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-(2-pyrimidinylamino)-5-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 746647-51-8 ZCAPLUS

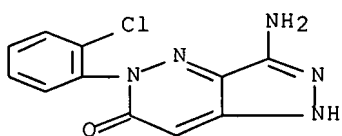
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-phenoxyphenyl)-3-(2-pyrimidinylamino)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

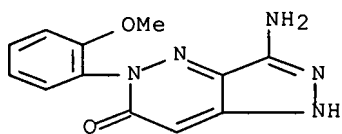
RN 746647-52-9 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-5-(2-chlorophenyl)-1,5-dihydro- (9CI) (CA INDEX NAME)



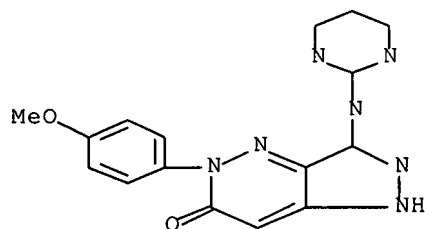
RN 746647-53-0 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 746647-54-1 ZCAPLUS

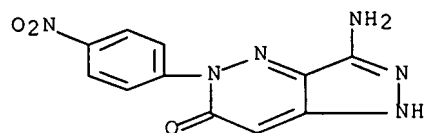
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-(2-pyrimidinylamino)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

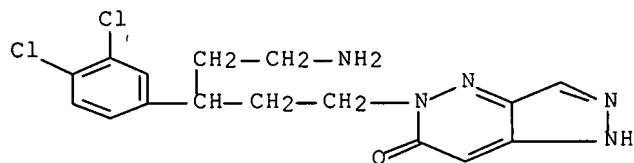
RN 746647-55-2 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



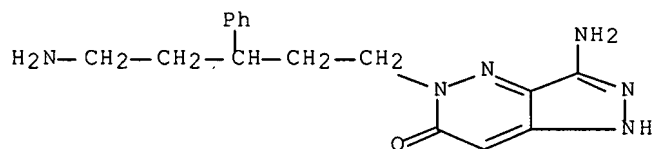
RN 746647-56-3 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dichlorophenyl)pentyl]-1,5-dihydro- (9CI) (CA INDEX NAME)



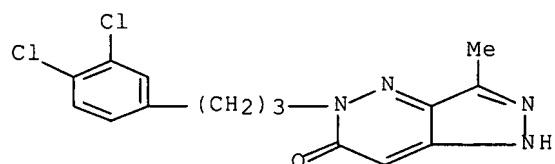
RN 746647-57-4 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-5-(5-amino-3-phenylpentyl)-1,5-dihydro- (9CI) (CA INDEX NAME)



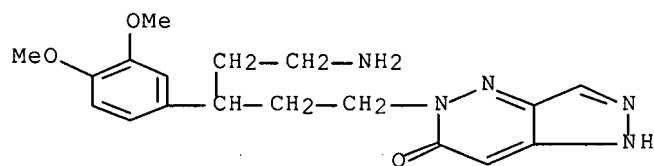
RN 746647-58-5 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[3-(3,4-dichlorophenyl)propyl]-1,5-dihydro-3-methyl- (9CI) (CA INDEX NAME)



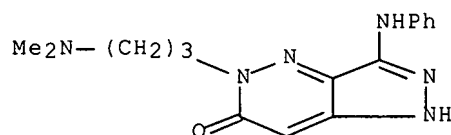
RN 746647-59-6 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dimethoxyphenyl)pentyl]-1,5-dihydro- (9CI) (CA INDEX NAME)



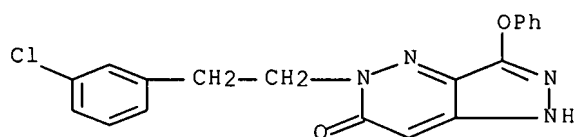
RN 746647-60-9 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[3-(dimethylamino)propyl]-1,5-dihydro-3-(phenylamino)- (9CI) (CA INDEX NAME)



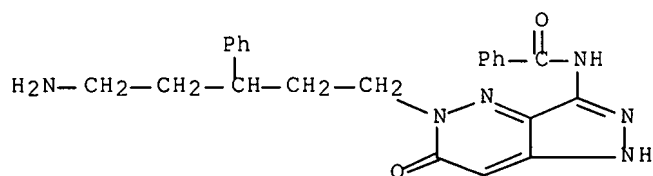
RN 746647-61-0 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[2-(3-chlorophenyl)ethyl]-1,5-dihydro-3-phenoxy- (9CI) (CA INDEX NAME)



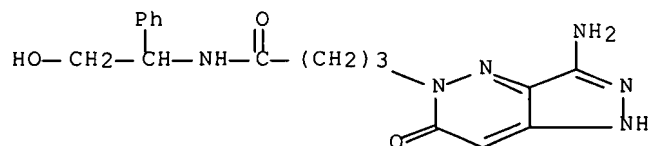
RN 746647-62-1 ZCAPLUS

CN Benzamide, N-[5-(5-amino-3-phenylpentyl)-5,6-dihydro-6-oxo-1H-pyrazolo[4,3-c]pyridazin-3-yl]- (9CI) (CA INDEX NAME)



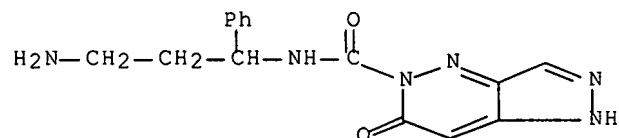
RN 746647-63-2 ZCAPLUS

CN 5H-Pyrazolo[4,3-c]pyridazine-5-butanamide, 3-amino-1,6-dihydro-N-(2-hydroxy-1-phenylethyl)-6-oxo- (9CI) (CA INDEX NAME)



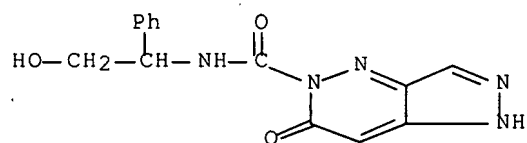
RN 746647-64-3 ZCAPLUS

CN 5H-Pyrazolo[4,3-c]pyridazine-5-carboxamide, N-(3-amino-1-phenylpropyl)-1,6-dihydro-6-oxo- (9CI) (CA INDEX NAME)



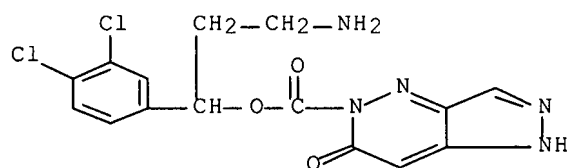
RN 746647-65-4 ZCAPLUS

CN 5H-Pyrazolo[4,3-c]pyridazine-5-carboxamide, 1,6-dihydro-N-(2-hydroxy-1-phenylethyl)-6-oxo- (9CI) (CA INDEX NAME)



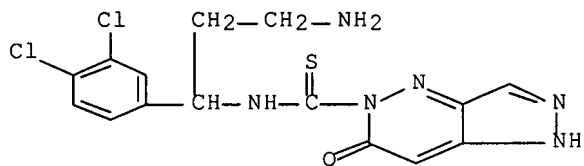
RN 746647-66-5 ZCAPLUS

CN 5H-Pyrazolo[4,3-c]pyridazine-5-carboxylic acid, 1,6-dihydro-6-oxo-, 3-amino-1-(3,4-dichlorophenyl)propyl ester (9CI) (CA INDEX NAME)



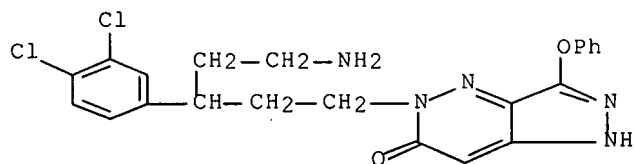
RN 746647-67-6 ZCAPLUS

CN 5H-Pyrazolo[4,3-c]pyridazine-5-carbothioamide, N-[3-amino-1-(3,4-dichlorophenyl)propyl]-1,6-dihydro-6-oxo- (9CI) (CA INDEX NAME)



RN 746647-68-7 ZCAPLUS

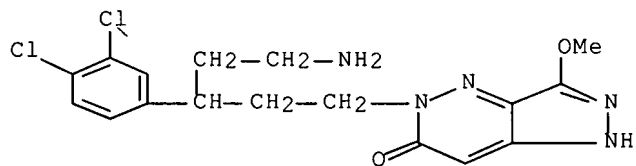
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dichlorophenyl)pentyl]-1,5-dihydro-3-phenoxy- (9CI) (CA INDEX NAME)



RN 746647-69-8 ZCAPLUS

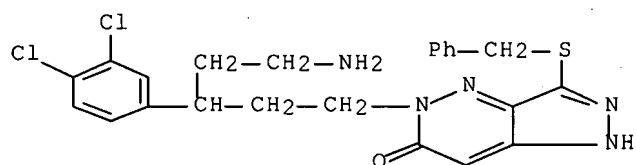
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dichlorophenyl)pentyl]-1,5-dihydro-3-methoxy- (9CI) (CA INDEX NAME)





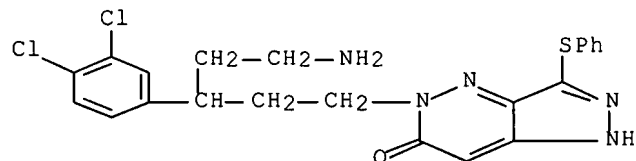
RN 746647-70-1 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dichlorophenyl)pentyl]-1,5-dihydro-3-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)



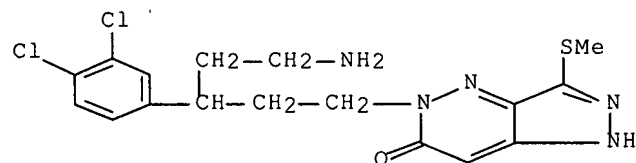
RN 746647-71-2 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dichlorophenyl)pentyl]-1,5-dihydro-3-(phenylthio)- (9CI) (CA INDEX NAME)



RN 746647-72-3 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[5-amino-3-(3,4-dichlorophenyl)pentyl]-1,5-dihydro-3-(methylthio)- (9CI) (CA INDEX NAME)

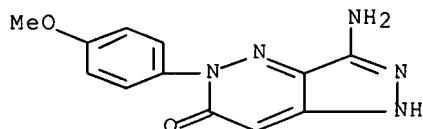


IT 338395-98-5

RL: RCT (Reactant); RACT (Reactant or reagent)  
(preparation of pyrazolopyridazines as inhibitors of protein kinases)

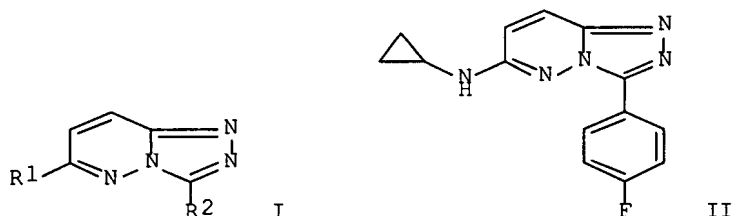
RN 338395-98-5 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-amino-1,5-dihydro-5-(4-methoxyphenyl)-  
(9CI) (CA INDEX NAME)



L14 ANSWER 5 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:566615 ZCAPLUS Full-text  
DOCUMENT NUMBER: 141:123634  
TITLE: A preparation of 2,3,7-triazaindolizine derivatives,  
useful as inhibitors of protein kinases  
INVENTOR(S): *Green, Jeremy; Grey, Ronald, Jr.;  
Pierce, Albert C.*  
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
SOURCE: PCT Int. Appl., 89 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004058769	A2	20040715	WO 2003-US39990	20031217
WO 2004058769	A3	20040930		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2510534	A1	20040715	CA 2003-2510534	20031217
AU 2003297161	A1	20040722	AU 2003-297161	20031217
US 2004192696	A1	20040930	US 2003-738956	20031217
EP 1575959	A2	20050921	EP 2003-814020	20031217
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1742012	A	20060301	CN 2003-80109129	20031217
JP 2006513208	T	20060420	JP 2004-563592	20031217
MX 2005PA06478	A	20050908	MX 2005-PA6478	20050616
NO 2005003470	A	20050902	NO 2005-3470	20050715
PRIORITY APPLN. INFO.:			US 2002-435124P	P 20021218
			WO 2003-US39990	W 20031217
OTHER SOURCE(S):	MARPAT 141:123634			
GI				



AB The invention relates to a preparation of 2,3,7-triazaindolizine derivs. of formula I [wherein: R1 is OR3, SR3, or NR3R4; R2 is -(T)O-1Ar; R3 and R4 are (U)O-1R5 or taken together with the nitrogen form 5-8 membered heterocycle ring; U is (un)substituted C1-6alkylidene chain; R5 is H, alkyl, or (hetero)aryl, etc.; T is NH or N-alkyl, etc.; Ar is 3-7 membered (un)saturated monocycle with 0-3 heteroatoms, etc.], or a pharmaceutically acceptable salt thereof. These compds. are inhibitors of protein kinases, particularly inhibitors of PIM-1, CDK-2, GSK-3, and SRC mammalian protein kinases. For instance, 2,3,7-triazaindolizine derivative II was screened for inhibition of PIM-1 (IC50 or Ki < 1.0  $\mu$ M) and GSK-3 (Ki < 2.0  $\mu$ M). The invention also provides pharmaceutically acceptable compns. comprising the compds. of the invention and methods of utilizing those compds. and compns. in the treatment of various protein kinase mediated disorders.

L14 ANSWER 6 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:453193 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:23537

TITLE: Preparation of 3,5-diamino[1,2,4]triazoles as protein kinase inhibitors

INVENTOR(S): **Pierce, Albert C.**; Arnost, Michael; Davies, Robert J.; Forster, Cornelia J.; Galullo, Vincent; **Grey, Ronald**; Ledeboer, Mark; Tian, Shi-kai; Xu, Jinwang; Binch, Hayley; Ledford, Brian; Messersmith, David; Nanthakumar, Suganthi; Jayaraj, Andrew

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 392 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

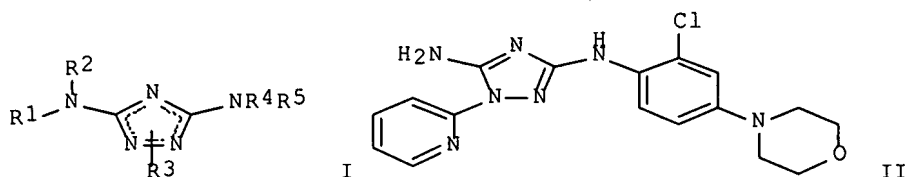
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004046120	A2	20040603	WO 2003-US36849	20031117
WO 2004046120	A3	20040812		

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UG, US, UZ, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,  
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2505789	A1	20040603	CA 2003-2505789	20031117
AU 2003294329	A1	20040615	AU 2003-294329	20031117
US 2004214817	A1	20041028	US 2003-715111	20031117
EP 1562589	A2	20050817	EP 2003-789812	20031117
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BR 2003016350	A	20050927	BR 2003-16350	20031117
CN 1738615	A	20060222	CN 2003-80108825	20031117
JP 2006515313	T	20060525	JP 2004-570619	20031117
NO 2005002888	A	20050812	NO 2005-2888	20050610
IN 2005KN01154	A	20061103	IN 2005-KN1154	20050615
PRIORITY APPLN. INFO.:			US 2002-426681P	P 20021115
			US 2003-447705P	P 20030211
			WO 2003-US36849	W 20031117

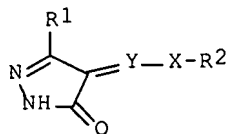
OTHER SOURCE(S): MARPAT 141:23537  
 GI



AB Title compds. I [wherein R<sup>1</sup> = H, YR'; Y = (un)substituted alkylidene wherein up to two methylene units are optionally and independently replaced with O, S, (un)substituted NH, OCO, CO<sub>2</sub>, CO; R' = independently H or (un)substituted aliphatic group, (hetero)cyclic ring; R<sup>2</sup> = TnAr<sup>1</sup>, TnCyl; R<sup>3</sup> = LmAr<sup>2</sup>, LmCy<sup>2</sup>; L, T = (un)substituted alkylidene wherein one methylene unit is optionally replaced by S, O, CS, CO<sub>2</sub>, OCO, CO, COCO, SO, SO<sub>2</sub>, PO, PO<sub>2</sub>, or (un)substituted NH, CONH, NHCO, NHCO<sub>2</sub>, SO<sub>2</sub>NH, NHSO<sub>2</sub>, CONHNH, NHCONH, OCONH, NHNH, NHSO<sub>2</sub>NH; m, n = 0-1; Ar<sup>1</sup>, Ar<sup>2</sup> = (un)substituted mono- or bicyclic (hetero)aryl; Cyl, Cy<sup>2</sup> = (un)substituted mono- or bicyclic aliphatic or heterocyclic ring; or NR<sup>1</sup>R<sup>2</sup> = (un)substituted heterocycle; R<sup>4</sup> = H, alkyl; with the proviso that when R<sup>5</sup> = H, then R<sup>4</sup> = H; R<sup>5</sup> = H; or R<sup>3</sup> and R<sup>5</sup> taken together form an (un)substituted (hetero)cycle; and pharmaceutically acceptable salts thereof] were prepared as inhibitors of the protein kinases FLT-3, FMS, c-KIT, PDGFR, JAK, AGC sub-family, CDK, GSK, SRC, ROCK, and/or SYK (no data). For example, cycloaddn. of N-cyano-N'-(2-chloro-4-morpholinophenyl)-O-phenylisourea and 2-hydrazinopyridine in i-PrOH gave II (79%). The invention also provides pharmaceutical compns. comprising the compds. of the invention and methods of using the compns. in the treatment of various disorders, such as cancer, Alzheimer's disease, restenosis, angiogenesis, glomerulonephritis, cytomegalovirus, HIV, herpes, psoriasis, atherosclerosis, alopecia, an autoimmune disease, a viral infection, a neurodegenerative disorder, a disorder associated with thymocyte apoptosis, a proliferative disorder, or a hematopoietic disorder (no data).

L14 ANSWER 7 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2003:117622 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 138:170229  
 TITLE: Preparation of pyrazolone derivatives as inhibitors of  
 GSK-3, Aurora-2 and CDK-2  
 INVENTOR(S): **Green, Jeremy**; Arnost, Michael J.;  
**Pierce, Albert**  
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
 SOURCE: PCT Int. Appl., 143 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011287	A1	20030213	WO 2002-US24726	20020802
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW	
RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
AU 2002330983	A1	20030217	AU 2002-330983	20020802
US 2004024040	A1	20040205	US 2002-212471	20020802
US 6916798	B2	20050712		
US 2005222237	A1	20051006	US 2005-145356	20050603
PRIORITY APPLN. INFO.:			US 2001-309838P	P 20010803
			US 2002-212471	A3 20020802
			WO 2002-US24726	W 20020802
OTHER SOURCE(S):		MARPAT 138:170229		
GI				



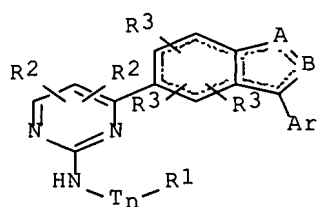
AB The present invention relates to pyrazolones (shown as I; variables defined below; e.g. 4-[(3-benzyloxyphenylamino)methylene]-5-(3,4- dimethoxyphenyl)-2,4-dihydropyrazol-3-one) that are useful as glycogen synthase kinase-3, Aurora-2 protein kinase and cyclin-dependent kinase-2 inhibitors (pharmacol. results included). The invention also relates to methods of using I or pharmaceutical compns. comprising I to inhibit the enzymes. The invention further provides methods of using these compds. and pharmaceutical compns. in the treatment and prevention of various disorders, such as diabetes and Alzheimer's disease. Although the methods of preparation are not claimed, .apprx.12 example prepn. are included and characterization data are included for .apprx.200 I. For I: R1 = H, alkyl, carbocyclyl, heterocyclyl, aryl,

heteroaryl, -CN, -C(O)R, -CO<sub>2</sub>R, or -CON(R)<sub>2</sub>; R<sub>2</sub> = H, alkyl, carbocyclyl, heterocyclyl, aryl, or heteroaryl; X is O, S or -NH; Y is N or CH; each R = H, alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, or any two R groups taken together form a carbocyclyl, heterocyclyl, aryl or heteroaryl group; each R' = H, alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, or any two R' groups taken together form a carbocyclyl, heterocyclyl, aryl or heteroaryl group; addnl. conditions are given in the claims.

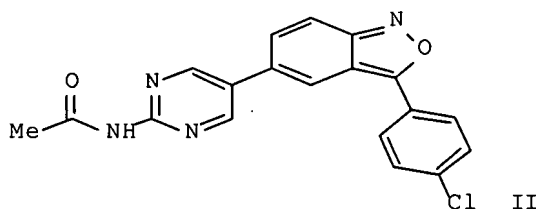
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:977814 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 138:39275  
 TITLE: Preparation of 5-(2-aminopyrimidin-4-yl)benzisoxazoles as protein kinase inhibitors  
 INVENTOR(S): Moon, Young Choon; **Green, Jeremy**; Davies, Robert; Choquette, Deb; **Pierce, Albert**; Ledebor, Mark  
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
 SOURCE: PCT Int. Appl., 88 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102800	A1	20021227	WO 2002-US19186	20020614
WO 2002102800	A9	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450769	A1	20021227	CA 2002-2450769	20020614
AU 2002344766	A1	20030102	AU 2002-344766	20020614
US 2004009996	A1	20040115	US 2002-172888	20020614
US 6825190	B2	20041130		
EP 1399440	A1	20040324	EP 2002-744399	20020614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005509592	T	20050414	JP 2003-506273	20020614
MX 2003PA11652	A	20040531	MX 2003-PA11652	20031215
US 2005228005	A1	20051013	US 2004-999128	20041129
PRIORITY APPLN. INFO.:			US 2001-298646P	P 20010615
			US 2002-172888	A3 20020614
			WO 2002-US19186	W 20020614
OTHER SOURCE(S):			MARPAT 138:39275	
GI				



I



II

AB Title compds. I [wherein AB = NO or ON; Ar = (un)substituted aryl; T = alkylidene chain wherein 1 or 2 methylene units may be independently replaced by O, NR, S, CO, CONR, NRCONR, SO<sub>2</sub>, SO<sub>2</sub>NR, NRSO<sub>2</sub>, NRSO<sub>2</sub>NR, CO<sub>2</sub>, OCO, NRCO<sub>2</sub>, or OCONR; n = 0-1; R<sub>1</sub> = H or (un)substituted aliphatic, aryl, aralkyl, or heterocyclyl(alkyl); R<sub>2</sub> and R<sub>3</sub> = independently R, halo, CN, OR, NR<sub>2</sub>, SR, COR, CO<sub>2</sub>R, CONR<sub>2</sub>, NRCOR, NRCO<sub>2</sub>-aliphatic, OCOR, SO<sub>2</sub>R, SOR, SO<sub>2</sub>NR<sub>2</sub>, or NRSO<sub>2</sub>-aliphatic; R = independently H or aliphatic; or NR<sub>2</sub> = heterocyclyl; or pharmaceutically acceptable derivs. or prodrugs thereof] were prepared as inhibitors of protein kinases, particularly inhibitors of glycogen synthase kinase-3 (GSK-3) and Janus kinase (JAK) mammalian protein kinases. For example, addition of a mixture of guanidine•HCl and 1-[3-(4-chlorophenyl)benzo[c]isoxazol-5-yl]-3-dimethylaminopropenone to Na pellets in MeOH followed by heating to 80° for 18 h gave 4-[3-(4-chlorophenyl)benzo[c]isoxazol-5-yl]pyrimidin-2-ylamine (98%), which was acylated to afford II (30%). Many of the compds. of the invention inhibited GSK-3 activity with K<sub>i</sub> values below 1 μM. The invention also provides pharmaceutically acceptable compns. comprising I and methods of using those compds. and compns. in the treatment of various protein kinase mediated disorders, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, asthma, inflammatory conditions, immunol. disorders, cardiovascular disease, liver disease, blood disorders, or immunodeficiency disorders (no data).

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:220583 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 136:247583  
 TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease  
 INVENTOR(S): Davies, Robert; Bebbington, David; Knegt, Ronald; Wannamaker, Marion; Li, Pan; Forester, Cornelia; **Pierce, Albert**; Kay, David  
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
 SOURCE: PCT Int. Appl., 373 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 14  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022607	A1	20020321	WO 2001-US28940	20010914
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
US, UZ, VN, YU, ZA, ZW  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2422379	A1	20020321	CA 2001-2422379	20010914
AU 200191013	A	20020326	AU 2001-91013	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
US 6638926	B2	20031028		
US 2003064981	A1	20030403	US 2001-952836	20010914
US 6613776	B2	20030902		
US 2003064982	A1	20030403	US 2001-952875	20010914
US 2003073687	A1	20030417	US 2001-952671	20010914
US 6660731	B2	20031209		
US 2003078166	A1	20030424	US 2001-955601	20010914
US 6696452	B2	20040224		
US 2003083327	A1	20030501	US 2001-952833	20010914
US 6610677	B2	20030826		
BR 2001014088	A	20030617	BR 2001-14088	20010914
EP 1318997	A1	20030618	EP 2001-971082	20010914
EP 1318997	B1	20060531		
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HU 200302173	A2	20030929	HU 2003-2173	20010914
ZA 2003001701	A	20040301	ZA 2003-1701	20010914
ZA 2003001703	A	20040302	ZA 2003-1703	20010914
JP 2004509117	T	20040325	JP 2002-526860	20010914
US 2004097501	A1	20040520	US 2001-953471	20010914
US 7115739	B2	20061003		
NZ 525008	A	20041224	NZ 2001-525008	20010914
US 2005004110	A1	20050106	US 2001-952878	20010914
US 7098330	B2	20060829		
ES 2242771	T3	20051116	ES 2001-1971006	20010914
AT 326458	T	20060615	AT 2001-970969	20010914
AT 327990	T	20060615	AT 2001-970971	20010914
AT 327992	T	20060615	AT 2001-971082	20010914
AT 327991	T	20060615	AT 2001-973050	20010914
AT 326459	T	20060615	AT 2001-977779	20010914
EP 1698627	A1	20060906	EP 2006-10798	20010914
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PT 1318997	T	20061031	PT 2001-971082	20010914
AT 346064	T	20061215	AT 2001-975210	20010914
ES 2266258	T3	20070301	ES 2001-1970971	20010914
ES 2266259	T3	20070301	ES 2001-1971082	20010914
CN 1926132	A	20070307	CN 2001-817434	20010914
AT 363284	T	20070615	AT 2001-977783	20010914
NZ 545284	A	20070629	NZ 1984-5452	20010914
CA 2432303	A1	20020829	CA 2001-2432303	20011219
AU 2002255452	A1	20020904	AU 2002-255452	20011219
CA 2432223	A1	20020906	CA 2001-2432223	20011219
AU 2001297619	A1	20020912	AU 2001-297619	20011219
EP 1345922	A1	20030924	EP 2001-271061	20011219
EP 1345922	B1	20060531		
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EP 1355905	A1	20031029	EP 2001-273861	20011219
EP 1355905	B1	20070221		



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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NZ 526472	A	20040430	NZ 2001-526472	20011219
JP 2004518743	T	20040624	JP 2002-565976	20011219
JP 2004519479	T	20040702	JP 2002-567928	20011219
HU 200400842	A2	20040728	HU 2004-842	20011219
NZ 526473	A	20050624	NZ 2001-526473	20011219
EP 1702920	A1	20060920	EP 2006-11799	20011219

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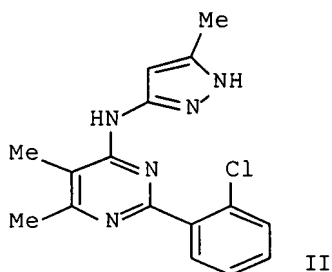
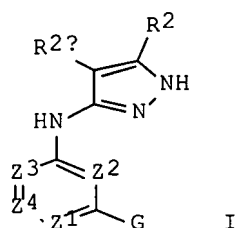
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ZA 2003001699	A	20040301	ZA 2003-1699	20030228
ZA 2003001700	A	20040301	ZA 2003-1700	20030228
ZA 2003001702	A	20040301	ZA 2003-1702	20030228
ZA 2003001704	A	20040301	ZA 2003-1704	20030228
ZA 2003001698	A	20040302	ZA 2003-1698	20030228
IN 2003KN00295	A	20060922	IN 2003-KN295	20030310
NO 2003001191	A	20030513	NO 2003-1191	20030314
MX 2003PA02291	A	20030606	MX 2003-PA2291	20030317
ZA 2003004468	A	20040624	ZA 2003-4468	20030609
ZA 2003004469	A	20040624	ZA 2003-4469	20030609
ZA 2003004470	A	20040624	ZA 2003-4470	20030609
ZA 2003004471	A	20040624	ZA 2003-4471	20030609
ZA 2003004473	A	20040624	ZA 2003-4473	20030609
ZA 2003004475	A	20040624	ZA 2003-4475	20030609
ZA 2003004472	A	20040625	ZA 2003-4472	20030609
ZA 2003004474	A	20040625	ZA 2003-4474	20030609
NO 2003002704	A	20030821	NO 2003-2704	20030613
MX 2003PA05609	A	20031006	MX 2003-PA5609	20030620
MX 2003PA05610	A	20031006	MX 2003-PA5610	20030620
US 2004224944	A1	20041111	US 2003-624800	20030722
US 7008948	B2	20060307		
US 2004116454	A1	20040617	US 2003-692355	20031023
US 2004157893	A1	20040812	US 2003-722374	20031125
US 2004132781	A1	20040708	US 2003-736426	20031215
US 7087603	B2	20060808		
HK 1058356	A1	20061201	HK 2003-109140	20031215
US 2004167141	A1	20040826	US 2004-775699	20040210
HK 1060347	A1	20061201	HK 2004-101883	20040315
JP 2005097322	A	20050414	JP 2004-366925	20041217
AU 2006201228	A1	20060413	AU 2006-201228	20060321
AU 2006201229	A1	20060413	AU 2006-201229	20060321
AU 2006201230	A1	20060413	AU 2006-201230	20060321
AU 2006201262	A1	20060427	AU 2006-201262	20060321
AU 2006201263	A1	20060427	AU 2006-201263	20060321
AU 2006201264	A1	20060427	AU 2006-201264	20060321
AU 2006201265	A1	20060427	AU 2006-201265	20060321
AU 2006201391	A1	20060427	AU 2006-201391	20060404
AU 2006201396	A1	20060504	AU 2006-201396	20060404
US 2006258658	A1	20061116	US 2006-492450	20060725

PRIORITY APPLN. INFO.:

US 2000-232795P	P	20000915
US 2000-257887P	P	20001221
US 2001-286949P	P	20010427
AU 2001-90944	A3	20010914
AU 2001-91013	A3	20010914
AU 2001-94558	A3	20010914
AU 2001-96871	A3	20010914
AU 2001-96875	A3	20010914
EP 2001-971082	A3	20010914
US 2001-952671	A3	20010914

US 2001-953471	A3 20010914
US 2001-955601	A3 20010914
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EP 2001-273861	A 20011219
EP 2001-994323	A3 20011219
JP 2002-557938	A3 20011219
US 2001-26966	A1 20011219
WO 2001-US49139	W 20011219
WO 2001-US50312	W 20011219
US 2001-34019	A3 20011220
US 2001-34683	A1 20011220

OTHER SOURCE(S): MARPAT 136:247583  
GI



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z<sub>1</sub> = N or CR<sub>9</sub>; Z<sub>2</sub> = N or CH; Z<sub>3</sub> = N or CR<sub>x</sub>; Z<sub>4</sub> = N or CR<sub>y</sub>; R<sub>x</sub> and R<sub>y</sub> = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R<sub>2</sub> and R<sub>2a</sub> = independently R, TWR<sub>6</sub>; or C<sub>2</sub>R<sub>2</sub>R<sub>2a</sub> = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>OCONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R<sub>3</sub> = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SO<sub>0</sub>-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R<sub>4</sub> = R<sub>7</sub>, COR<sub>7</sub>, CO<sub>2</sub>(aliphatic), CON(R<sub>7</sub>)<sub>2</sub>, or SO<sub>2</sub>R<sub>7</sub>; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>6</sub> and R<sub>7</sub> = independently H or (un)substituted aliphatic group; or N(R<sub>6</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; or N(R<sub>7</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>9</sub> = R, halo, OR, COR, CO<sub>2</sub>R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z<sub>1</sub> and Z<sub>2</sub> = N; Z<sub>3</sub> = CR<sub>x</sub>; Z<sub>4</sub> = CR<sub>y</sub>; G = Ring C]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β<sub>3</sub>, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3β) and 0.1-1.0 μM for Aurora-2.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine  
404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine

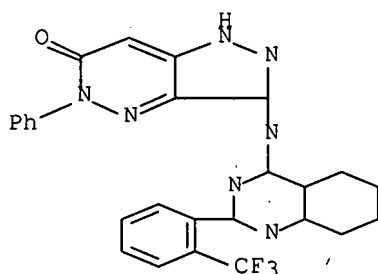
**404829-17-0P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine **404829-18-1P**, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-19-2P**, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-21-6P**, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-22-7P**, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-23-8P**, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 ZCAPLUS

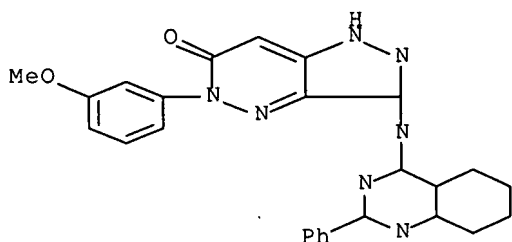
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 ZCAPLUS

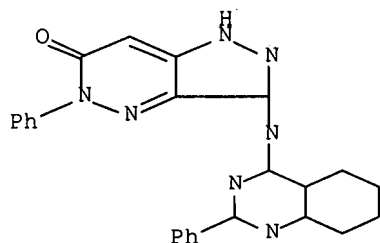
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 ZCAPLUS

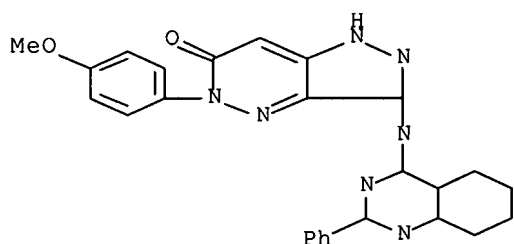
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 ZCAPLUS

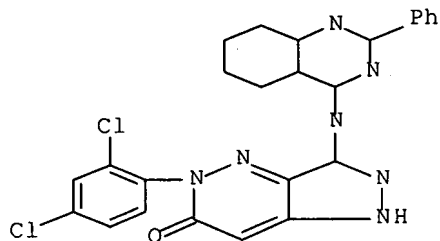
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 ZCAPLUS

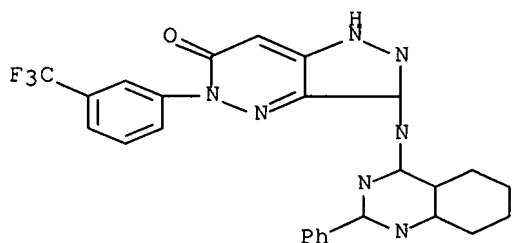
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 ZCAPLUS

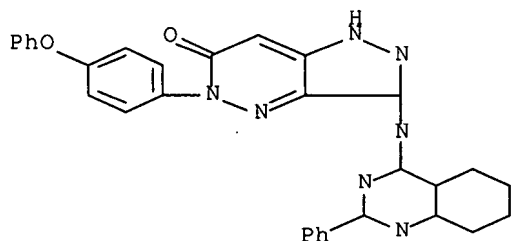
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 ZCAPLUS

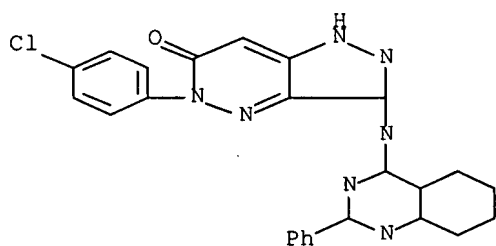
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:220582 ZCAPLUS Full-text

DOCUMENT NUMBER: 136:247582

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Binch, Hayley; Knegtel, Ronald;  
 Golec, Julian M. C.; Patel, Sanjay; Charrier,  
 Jean-Damien; Kay, David; Davies, Robert; Li, Pan;  
 Wannamaker, Marion; Forster, Cornelia; **Pierce,**  
**Albert**

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 355 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

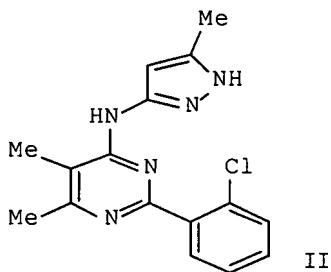
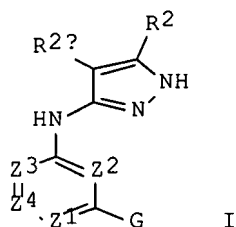
PATENT INFORMATION:

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US 2003064981	A1	20030403	US 2001-952836	20010914
US 6613776	B2	20030902		
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			WO 2001-US50312	W 20011219
			US 2001-34019	A3 20011220
			US 2001-34683	A1 20011220

OTHER SOURCE(S): MARPAT 136:247582  
GI



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; R<sub>x</sub> and R<sub>y</sub> = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR<sub>6</sub>; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>OCONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R<sub>3</sub> = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SO<sub>0</sub>-2R,



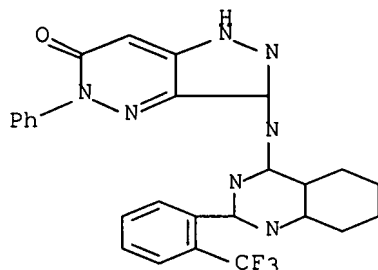
N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.) were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRy; G = Ring D]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- $\beta$ 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1  $\mu$ M for glycogen synthetase kinase 3 $\beta$  (GSK-3 $\beta$ ) and 0.1-1.0  $\mu$ M for Aurora-2.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine  
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 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 ZCAPLUS

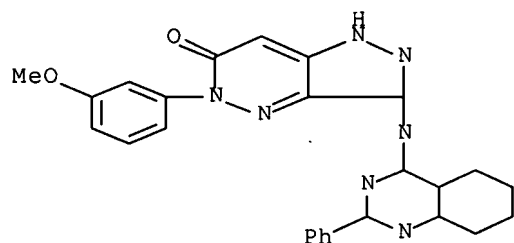
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 ZCAPLUS

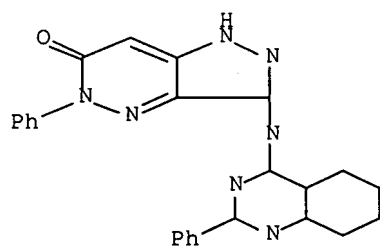
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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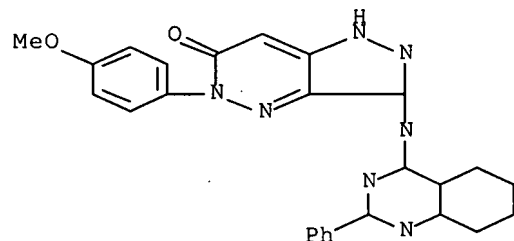
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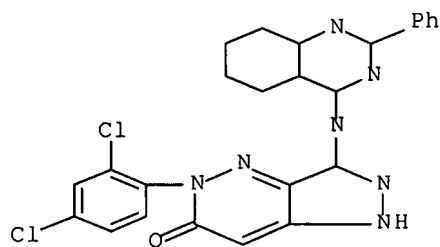
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RN 404829-19-2 ZCAPLUS

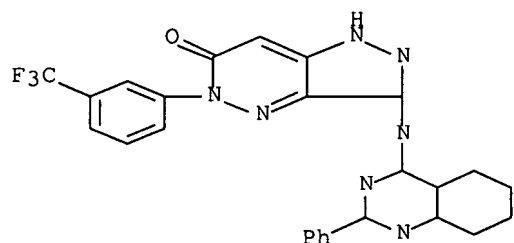
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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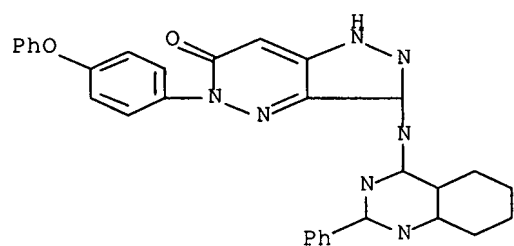
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 ZCAPLUS

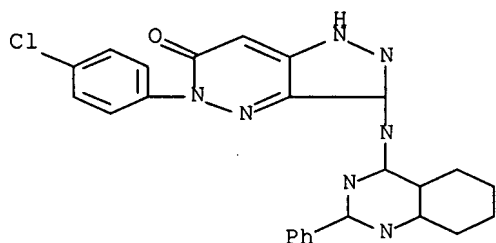
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 11 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:220577 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 136:247579  
 TITLE: Preparation of pyrazolamines and analogs as protein  
 kinase inhibitors for treatment of cancer, diabetes,  
 and Alzheimer's disease  
 INVENTOR(S): Knegt, Ronald; Bebbington, David; Binch, Hayley;  
 Golec, Julian; Patel, Sanjay; Charrier, Jean-Damien;  
 Kay, David; Davies, Robert; Li, Pan; Wannamaker,  
 Marion; Forster, Cornelia; **Pierce, Albert**  
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
 SOURCE: PCT Int. Appl., 376 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 14  
 PATENT INFORMATION:

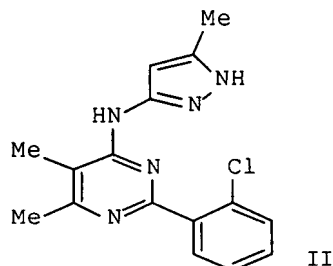
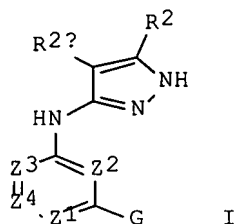
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022601	A1	20020321	WO 2001-US28740	20010914
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US 6613776	B2	20030902		
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US 6660731	B2	20031209		
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EP 1317444	A1	20030611	EP 2001-970971	20010914
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			WO 2001-US49139	W 20011219
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			US 2001-34019	A3 20011220
			US 2001-34683	A1 20011220

OTHER SOURCE(S):  
GI

MARPAT 136:247579



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; R<sub>x</sub> and R<sub>y</sub> = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR<sub>6</sub>; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>CONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R<sub>3</sub> = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SOO-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R<sub>4</sub> = R<sub>7</sub>, COR<sub>7</sub>, CO<sub>2</sub>(aliphatic), CON(R<sub>7</sub>)<sub>2</sub>, or SO<sub>2</sub>R<sub>7</sub>; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>6</sub> and R<sub>7</sub> = independently H or (un)substituted aliphatic group; or N(R<sub>6</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; or N(R<sub>7</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>9</sub> = R, halo, OR, COR, CO<sub>2</sub>R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrimidinyl- and pyridinyl- pyrazolamines and indazolamines I [wherein Z1 = N, CR<sub>a</sub>, or CH; Z2 = N or CH; and at least one of Z1 or Z2 = N; Z3 = CR<sub>x</sub>; Z4 = CR<sub>y</sub>; R<sub>a</sub> = halo, OR, COR, CO<sub>2</sub>R, COCOR, NO<sub>2</sub>, CN, SOO-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, etc.; R and R<sub>4</sub> are defined above]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited K<sub>i</sub> values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3β) and 0.1-1.0 μM for Aurora-2.

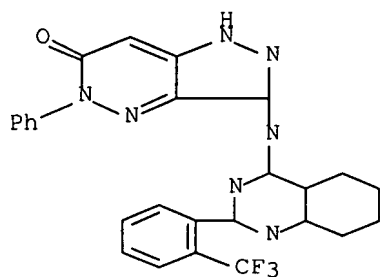
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

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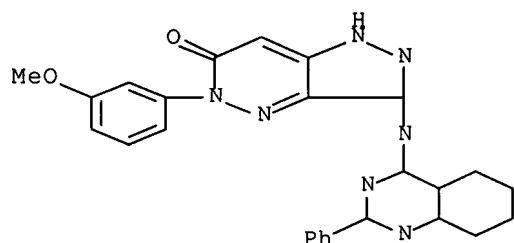
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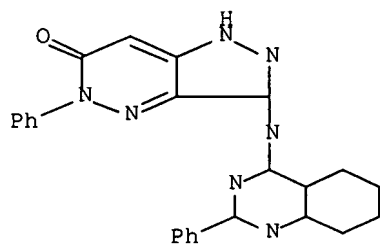
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RN 404829-17-0 ZCAPLUS

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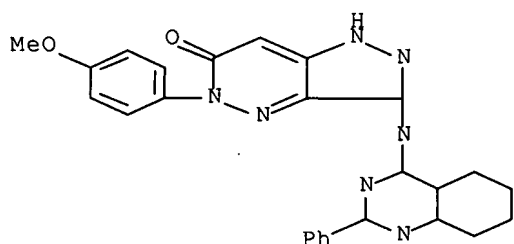


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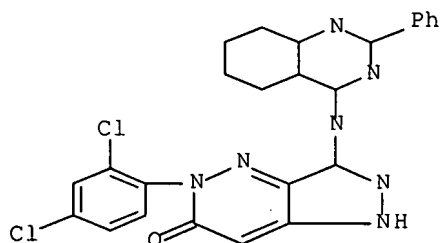




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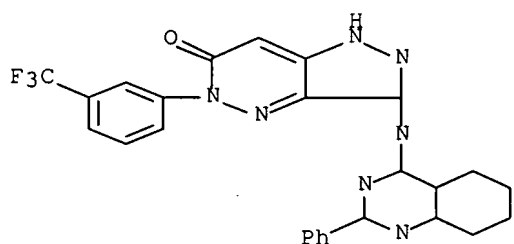
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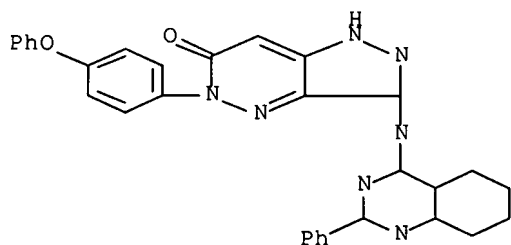
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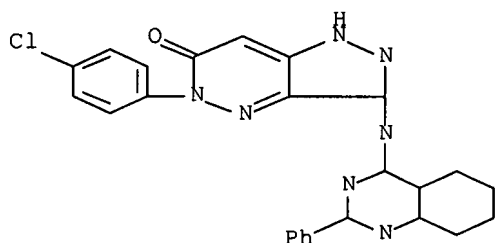
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 1 OF 3 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 141:225525 MARPAT Full-text

TITLE: Preparation of pyrazolopyridazines as inhibitors of protein kinases

INVENTOR(S): Green, Jeremy; Grey, Ronald; Pierce, Albert C.

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO 2004072029	A3	20041216		

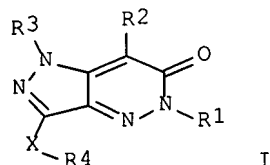
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BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,  
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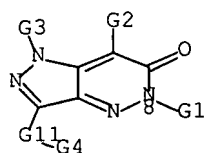
US 2004-772219 20040204  
 US 2003-445529P 20030206  
 WO 2004-US3061 20040204

GI



AB The title compds. [I; R1 = substituted Ph, alkylphenyl, CH2Ph, etc.; R2 = halo, NO2, CN, etc.; R3 = H, alkyl; X = a bond, O, S, (un)unsubstituted NH; R4 = H, quinazolinyl, pyrimidinyl, etc.] which are inhibitors of protein kinases, particularly inhibitors of GSK mammalian protein kinase, and more particularly inhibitors of GSK-3 mammalian protein kinase, were prepared E.g., a multi-step synthesis of 3-amino-5-(3,4-dimethoxyphenyl)-1,5-dihydropyrazolo[4,3-c]pyridazine-6-one, starting from 3,4-dimethoxyaniline and di-Me acetonediacarboxylate, was given. The representative compds. I were shown to have Ki of < 4.0  $\mu$ M for GSK-3 $\beta$ . The invention also provides pharmaceutically acceptable compns. comprising the compds. I and methods of utilizing those compds. and compns. in the treatment of various protein kinase mediated disorders.

#### MSTR 1



G11 = bond

Patent location:

Note:

Note:

Note:

Note:

claim 1

or pharmaceutically acceptable salts

substitution is restricted

additional ring formation also claimed

additional heteroatom interruptions also claimed

L30 ANSWER 2 OF 3 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 136:247583 MARPAT [Full-text](#)

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Davies, Robert; Bebbington, David; Knegetel, Ronald;  
Wannamaker, Marion; Li, Pan; Forester, Cornelia;  
Pierce, Albert; Kay, David  
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
SOURCE: PCT Int. Appl., 373 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 14  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022607	A1	20020321	WO 2001-US28940	20010914
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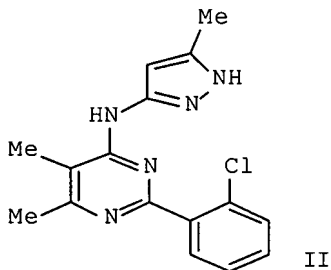
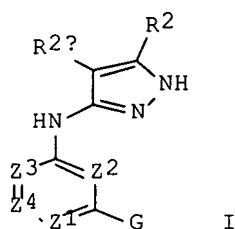
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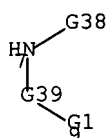
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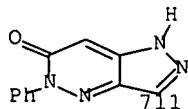
AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; Rx and Ry = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR<sub>6</sub>; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>CONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SOO-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R4 = R7, COR7, CO<sub>2</sub>(aliphatic), CON(R7)<sub>2</sub>, or SO<sub>2</sub>R7; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or

heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRy; G = Ring C]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- $\beta$ 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1  $\mu$ M for glycogen synthetase kinase 3 $\beta$  (GSK-3 $\beta$ ) and 0.1-1.0  $\mu$ M for Aurora-2.

#### MSTR 1A



G38 = 711



Patent location:

Note:

Note:

Note:

Note:

claim 1

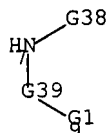
or pharmaceutically acceptable derivatives or prodrugs

also incorporates claim 30, formula C

also incorporates broader disclosure

additional fused ring formation also claimed

#### MSTR 1B



G38 = 711

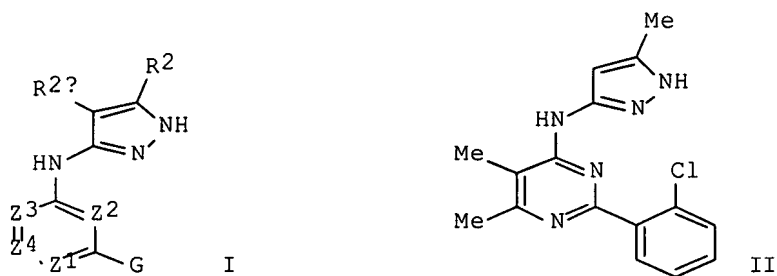




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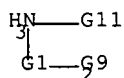
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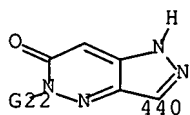


AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; R<sub>x</sub> and R<sub>y</sub> = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR<sub>6</sub>; or C<sub>2</sub>R<sub>2</sub>R<sub>2a</sub> = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>OCONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R<sub>3</sub> = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SOO-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R<sub>4</sub> = R<sub>7</sub>, COR<sub>7</sub>, CO<sub>2</sub>(aliphatic), CON(R<sub>7</sub>)<sub>2</sub>, or SO<sub>2</sub>R<sub>7</sub>; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>6</sub> and R<sub>7</sub> = independently H or (un)substituted aliphatic group; or N(R<sub>6</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; or N(R<sub>7</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>9</sub> = R, halo, OR, COR, CO<sub>2</sub>R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CR<sub>x</sub>; Z4 = CR<sub>y</sub>; G = Ring D]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited K<sub>i</sub> values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3β) and 0.1-1.0 μM for Aurora-2.

#### MSTR 1A

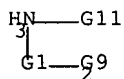


G11 = 440

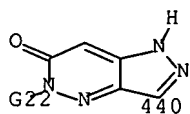


Patent location: claim 1  
 Note: also incorporates broader disclosure  
 Note: or pharmaceutically acceptable derivatives or prodrugs  
 Note: substitution is restricted  
 Note: additional ring formation also claimed

**MSTR 1B**



G11 = 440



Patent location: claim 1  
 Note: also incorporates broader disclosure  
 Note: or pharmaceutically acceptable derivatives or prodrugs  
 Note: substitution is restricted  
 Note: additional ring formation also claimed

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file registry

FILE 'REGISTRY' ENTERED AT 11:37:47 ON 20 AUG 2007

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STRUCTURE FILE UPDATES: 19 AUG 2007 HIGHEST RN 944998-48-5

DICTIONARY FILE UPDATES: 19 AUG 2007 HIGHEST RN 944998-48-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

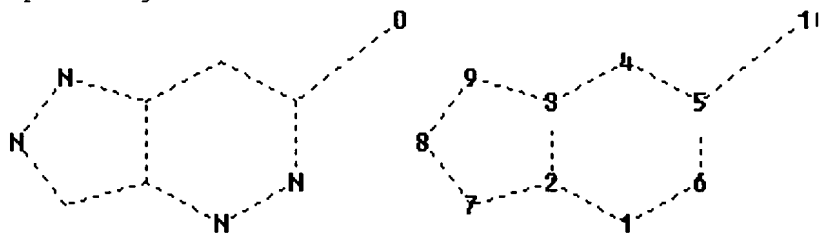
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdoc/properties.html>

Uploading L3.str



chain nodes :

10

ring nodes :

1 2 3 4 5 6 7 8 9

chain bonds :

5-10

ring bonds :

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 7-8 8-9

exact/norm bonds :

1-2 1-6 2-3 2-7 3-4 3-9 4-5 5-6 5-10 7-8 8-9

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

=> file zcaplus

FILE 'ZCAPLUS' ENTERED AT 11:38:04 ON 20 AUG 2007

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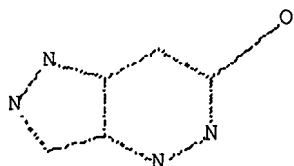
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FILE COVERS 1907 - 20 Aug 2007 VOL 147 ISS 9  
FILE LAST UPDATED: 19 Aug 2007 (20070819/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.  
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

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L3 STR



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L6 17 SEA FILE=ZCAPLUS ABB=ON PLU=ON L5

=> s L6 not L14  
L36 13 L6 NOT L14

=> file babs  
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FILE LAST UPDATED: 25 JUN 2007 <20070625/UP>  
FILE COVERS 1980 TO DATE.

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OR 5794913/BABSAN)

=> file marpat

FILE 'MARPAT' ENTERED AT 11:38:34 ON 20 AUG 2007  
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FILE CONTENT: 1961-PRESENT VOL 147 ISS 7 (20070817/ED)

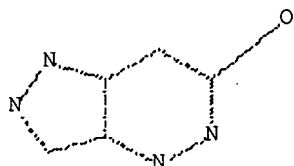
SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2007155779	05 JUL 2007
DE	102005063244	28 JUN 2007
EP	1801190	27 JUN 2007
JP	2007173472	05 JUL 2007
WO	2007076379	05 JUL 2007
GB	2433499	27 JUN 2007
FR	2895408	29 JUN 2007
RU	2302407	10 JUL 2007
CA	2571093	16 JUN 2007

Expanded G-group definition display now available.

=> d stat que L29  
L3 STR



Structure attributes must be viewed using STN Express query preparation.

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L9	422	SEA	FILE=ZCAPLUS	ABB=ON	PLU=ON	PIERCE A?/AU
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FILE 'MARPAT' ENTERED AT 11:39:11 ON 20 AUG 2007  
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 PROCESSING COMPLETED FOR L29  
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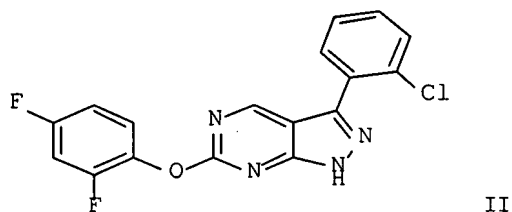
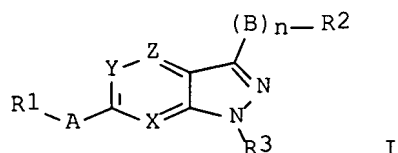
ANSWERS '1-13' FROM FILE ZCAPLUS  
 ANSWERS '14-39' FROM FILE MARPAT  
 ANSWER '40' FROM FILE BABS

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L37 ANSWER 1 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1  
 ACCESSION NUMBER: 2005:1004746 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 143:306308  
 TITLE: Preparation of heteroaryl-fused pyrazolo derivatives  
 as inhibitors of p38 kinase  
 INVENTOR(S): Arora, Nidhi; Billedeau, Roland J.; Dewdney, Nolan  
 James; Gabriel, Tobias; Goldstein, David Michael;  
 Soth, Michael; Trejo-Martin, Teresa Alejandra  
 PATENT ASSIGNEE(S): F.Hoffmann-La Roche AG, Switz.  
 SOURCE: PCT Int. Appl., 73 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005085248	A1	20050915	WO 2005-EP1815	20050222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2005219517	A1	20050915	AU 2005-219517	20050222
CA 2558109	A1	20050915	CA 2005-2558109	20050222
EP 1720878	A1	20061115	EP 2005-715442	20050222
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1934111	A	20070321	CN 2005-80006345	20050222
BR 2005008220	A	20070717	BR 2005-8220	20050222
US 2005203091	A1	20050915	US 2005-65890	20050225
IN 2006CN03092	A	20070518	IN 2006-CN3092	20060825
NO 2006004000	A	20060922	NO 2006-4000	20060906
PRIORITY APPLN. INFO.:			US 2004-548642P	P 20040227
			WO 2005-EP1815	W 20050222
OTHER SOURCE(S):		MARPAT 143:306308		
GI				





AB Title compds. I [R1 = (un)substituted aryl, heteroaryl or cycloalkyl; R2 = (un)substituted aryl, heteroaryl, alkyl, etc.; R3 = H or alkyl; one or two of X, Y and Z is N, and the other is CR4; R4 independently = H, alkyl, halo, etc.; A = O, CO, CH2, etc.; n = 0-1; B = O, CO, CH=CH, etc.] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of p38 kinase. Thus, e.g., II was prepared by cyclization of (2-chlorophenyl)-(4-chloro-2-methylsulfonylpyrimidin-5-yl)-methanone (preparation given) with hydrazine followed by oxidation to the resp. sulfonyl derivative and subsequent coupling with 2,4-difluorophenol. The inhibitory activity of I against p38 kinase was determined by measuring the transfer of the  $\gamma$ -phosphate from  $\gamma$ -33P-ATP by p38 kinase to Myelin Basic Protein (MBP) and it was revealed that compds. of the invention were inhibitors of p38 kinase, with one compound displaying an IC50 value of approx. 0.01  $\mu$ M. I as inhibitors of p38 kinase should prove useful in the treatment of arthritis, Crohn's disease or chronic obstructive pulmonary disease. Pharmaceutical compns. comprising I are disclosed.

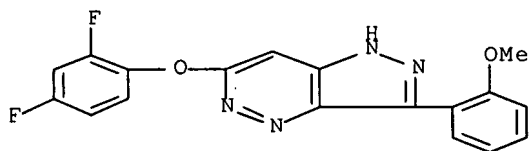
IT **864542-61-0P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heteroaryl-fused pyrazolo derivs. as inhibitors of p38 kinase)

RN 864542-61-0 ZCAPLUS

CN 1H-Pyrazolo[4,3-c]pyridazine, 6-(2,4-difluorophenoxy)-3-(2-methoxyphenyl)- (CA INDEX NAME)



REFERENCE COUNT:

8

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 2 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2  
 ACCESSION NUMBER: 2002:220580 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 136:247606  
 TITLE: Preparation of 3-(4-pyrimidinylamino)pyrazole  
 derivatives as protein kinase inhibitors, especially  
 of Aurora-2 and GSK-3, for treating cancer, diabetes  
 and Alzheimer's disease.  
 INVENTOR(S): Davies, Robert; Bebbington, David; Binch, Haley;  
 Knegetel, Ronald; Golec, Julian M. C.; Patel, Sanjay;  
 Charrier, Jean-Damien; Kay, David; Davies, Robert  
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
 SOURCE: PCT Int. Appl., 357 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 14  
 PATENT INFORMATION:

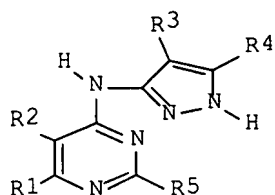
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US 2003055044	A1	20030320	US 2001-953505	20010914
US 6638926	B2	20031028		
US 2003064981	A1	20030403	US 2001-952836	20010914
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US 2003064982	A1	20030403	US 2001-952875	20010914
US 2003073687	A1	20030417	US 2001-952671	20010914
US 6660731	B2	20031209		
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EP 1698627	A1	20060906	EP 2006-10798	20010914
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EP 1345922	B1	20060531		
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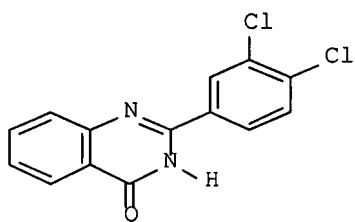
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AU 2006201228	A1	20060413	AU 2006-201228	20060321
AU 2006201229	A1	20060413	AU 2006-201229	20060321
AU 2006201230	A1	20060413	AU 2006-201230	20060321
AU 2006201262	A1	20060427	AU 2006-201262	20060321
AU 2006201263	A1	20060427	AU 2006-201263	20060321
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US 2006258658	A1	20061116	US 2006-492450	20060725
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			AU 2001-96871	A3 20010914
			AU 2001-96875	A3 20010914
			EP 2001-971082	A3 20010914
			US 2001-952671	A3 20010914
			US 2001-953471	A3 20010914
			US 2001-955601	A3 20010914
			WO 2001-US28792	W 20010914
			EP 2001-273861	A 20011219
			EP 2001-994323	A3 20011219
			JP 2002-557938	A3 20011219
			US 2001-26966	A1 20011219
			WO 2001-US49139	W 20011219
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			US 2001-34019	A3 20011220
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OTHER SOURCE(S): MARPAT 136:247606

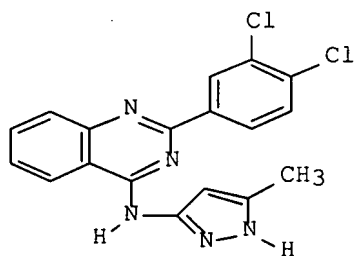
GI



I



II



III

AB The preparation of title compds. I and their pharmaceutically acceptable salts or prodrugs is described [wherein: R1, R2 = dependently form (un)substituted fused, unsatd. or partially unsatd., 5-8 membered carbocyclo ring; R3, R4 = independently H, aliphatic, aryl, heteroaryl, heterocyclyl, or wide variety of functionalized sidechains; or dependently form a fused, 5-8 membered, unsatd. or partially unsatd. ring having 0-3 ring heteroatoms (N, S, O); R5 = fused, (un)substituted 5-7 membered monocyclic ring or 8-10 membered bicyclic ring (aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms (N, S, O))]. For example, chlorination of quinazoline II with phosphorus oxychloride, followed by condensation with 3-amino-5-methylpyrazole afforded claimed compound III. Compds. I are inhibitors of GSK-3 and Aurora-2 protein kinases. The invention also relates to methods of treating diseases associated with these protein kinases, such as diabetes, cancer and Alzheimer's disease. In bioassays, compds. I inhibited the following kinases with Kis reported < 100 nM: GSK-3 $\beta$  (163 compds.), AURORA-2 (65 compds.), CDK-2 (no data), ERK2 (8 compds.), AKT (no data), and Human Src kinase (21 compds.). Claims included 146 specific compds., and 188 examples were given. The syntheses of 6 compds. and 46 intermediates are described.

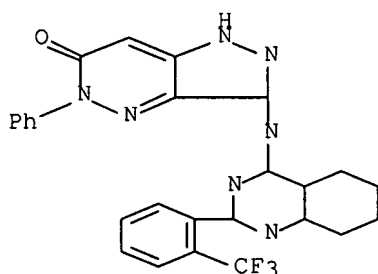
IT 404827-31-2P 404829-16-9P 404829-17-0P  
404829-18-1P 404829-19-2P 404829-21-6P  
404829-22-7P 404829-23-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-(4-pyrimidinylamino)pyrazole compds. as protein kinase inhibitors)

RN 404827-31-2 ZCAPLUS

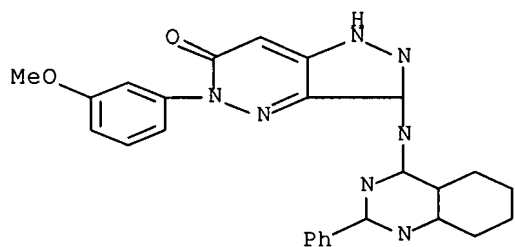
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



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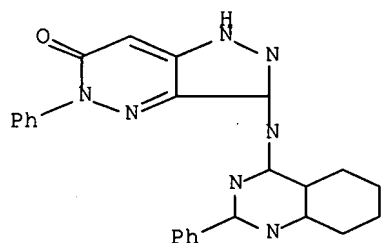
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[[2-phenyl-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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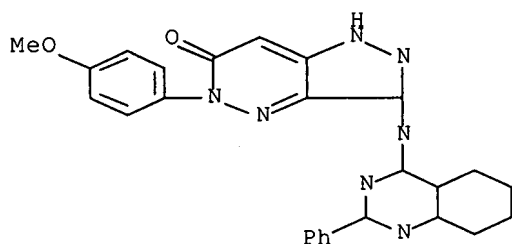
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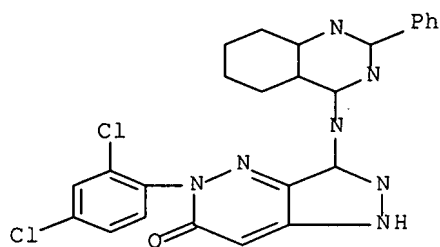
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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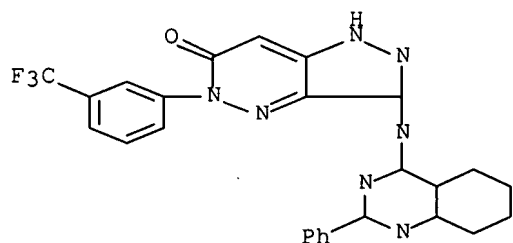
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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RN 404829-21-6 ZCAPLUS

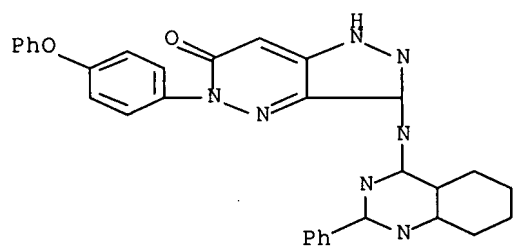
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 ZCAPLUS

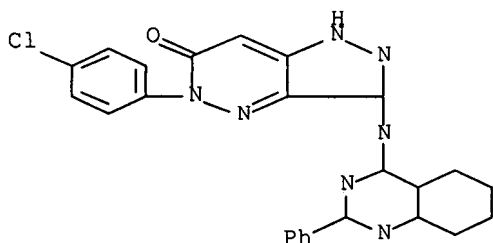
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

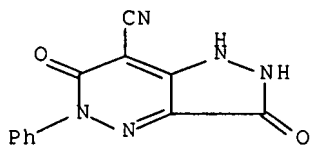
RN 404829-23-8 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



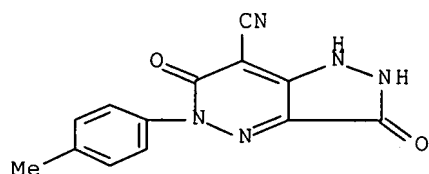
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE  
 REFERENCE COUNT: 5 ~~THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS~~  
~~RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT~~

137 ANSWER 3 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3  
 ACCESSION NUMBER: 1990:158181 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 112:158181  
 TITLE: Synthesis of polyfunctionally substituted pyridazines  
 AUTHOR(S): Ghozlan, Said Ahmed Soliman; Mohamed, Mona Hassan;  
 Fakhr, Yehia; Elnagdi, Mohamed Hilmy  
 CORPORATE SOURCE: Fac. Sci., Cairo Univ., Giza, Egypt  
 SOURCE: Liebigs Annalen der Chemie (1990), (3), 293-6  
 CODEN: LACHDL; ISSN: 0170-2041  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 112:158181  
 GI For diagram(s), see printed CA Issue.  
 AB Pyridazines, e.g. I (X = O, NH, NAc, R = CO<sub>2</sub>Et, cyano, R<sub>1</sub> = Ph, 4-MeC<sub>6</sub>H<sub>4</sub>),  
 were obtained by cyclization of hydrazone derivs. R<sub>1</sub>NHN:CRC(NH<sub>2</sub>):CRCN. (II)  
 with several reagents. Treatment of I (X = O, R = CONHNH<sub>2</sub>, R<sub>1</sub> = Ph, 4-MeC<sub>6</sub>H<sub>4</sub>)  
 with AcOH-HCl gave pyrazolo[4,3-c]pyridazine. Pyridopyridazine derivs. were  
 obtained by reaction of II and I with H<sub>2</sub>C(CN)<sub>2</sub> and EtO<sub>2</sub>CCH<sub>2</sub>CN, resp. and  
 isoxazolopyridazines by reaction of I with NH<sub>2</sub>OH.HCl in ethanolic NaOEt. The  
 intermediate in the reaction of I with NH<sub>2</sub>OH.HCl in ethanolic NaOAc was also  
 separated and characterized.  
 IT 123775-55-3P 123775-56-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 123775-55-3 ZCAPLUS  
 CN 1H-Pyrazolo[4,3-c]pyridazine-7-carbonitrile, 2,3,5,6-tetrahydro-3,6-dioxo-  
 5-phenyl- (9CI) (CA INDEX NAME)

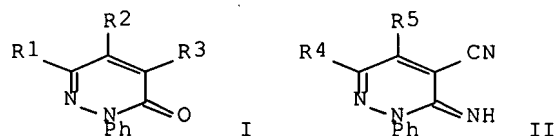


RN 123775-56-4 ZCAPLUS  
 CN 1H-Pyrazolo[4,3-c]pyridazine-7-carbonitrile, 2,3,5,6-tetrahydro-5-(4-  
 methylphenyl)-3,6-dioxo- (9CI) (CA INDEX NAME)





L37 ANSWER 4 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4  
 ACCESSION NUMBER: 1990:20955 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 112:20955  
 TITLE: Reactions with 3-oxo-2-phenylhydrazonobutyronitrile:  
 new routes for the synthesis of pyridazines  
 AUTHOR(S): Ghozlan, Said Ahmed Soliman; Mohamed, Mona Hassan;  
 Soliman, Ahmed Yousef; Bakeer, Hadir  
 CORPORATE SOURCE: Fac. Sci., Cairo Univ., Giza, Egypt  
 SOURCE: Gazzetta Chimica Italiana (1989), 119(2), 95-7  
 CODEN: GCITA9; ISSN: 0016-5603  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 112:20955  
 GI



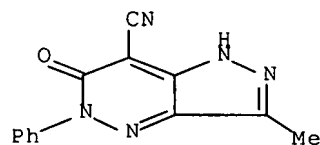
AB Pyridazines I (R1 = cyano, MeCO; R2 = Me, NH<sub>2</sub>; R3 = MeCO, cyano) and II (R4 = MeCO, cyano, R5 = NH<sub>2</sub>, Me) were prepared. A mixture of MeCOC(:NNHPh)CN (III) and NCCH<sub>2</sub>CO<sub>2</sub>Et was heated to give I (R1 = MeCO, R2 = NH<sub>2</sub>, R3 = cyano); III was treated with MeCOCH<sub>2</sub>CO<sub>2</sub>Et and NH<sub>4</sub>OAc to give I (R1 = cyano, R2 = Me, R3 = MeCO). II were obtained from III and CH<sub>2</sub>(CN)<sub>2</sub>.

IT **124315-59-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

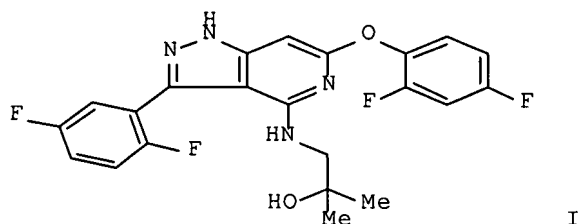
RN 124315-59-9 ZCAPLUS

CN 1H-Pyrazolo[4,3-c]pyridazine-7-carbonitrile, 5,6-dihydro-3-methyl-6-oxo-5-phenyl- (9CI) (CA INDEX NAME)



L37 ANSWER 5 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2007:226977 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 146:295911  
 TITLE: Preparation of fused pyrazole derivatives as P38 MAP  
 kinase inhibitors  
 INVENTOR(S): Arora, Nidhi; Billedeau, Roland Joseph; Dewdney, Nolan  
 James; Gabriel, Tobias; Goldstein, David Michael;  
 O'Yang, Counde; Soth, Michael; Trejo-Martin, Teresa  
 Alejandra  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 100pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007023105	A1	20070301	WO 2006-EP65297	20060815
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2005-712012P	P 20050825
GI				



AB The title fused pyrazole derivs. are prepared as p38 MAP kinase inhibitors for the treatment of p38-mediated diseases. For example, the compound I was prepared in a multi-step synthesis. I inhibited p38 MAP kinase with IC50 of 0.001  $\mu$ M in vitro. Formulations containing the title compound as an active ingredient were also described.

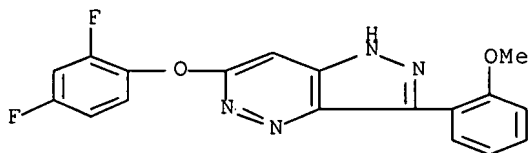
IT **864542-61-OP**  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(drug candidate; preparation of fused pyrazole derivs. as P38 MAP kinase  
inhibitors)

RN 864542-61-0 ZCAPLUS

CN 1H-Pyrazolo[4,3-c]pyridazine, 6-(2,4-difluorophenoxy)-3-(2-methoxyphenyl)-  
(CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 6 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:220584 ZCAPLUS Full-text

DOCUMENT NUMBER: 136:247584

TITLE: Preparation of pyrazolamines and analogs as protein  
kinase inhibitors for treatment of cancer, diabetes,  
and Alzheimer's disease

INVENTOR(S): Bebbington, David; Knegt, Ronald; Golec, Julian M.  
C.; Li, Pan; Davies, Robert; Charrier, Jean-Damien

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 356 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

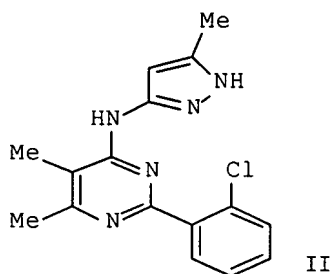
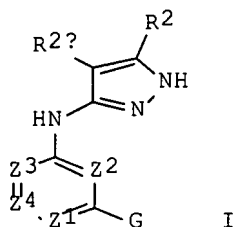
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022608	A1	20020321	WO 2001-US42152	20010914
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AU 200196871	A	20020326	AU 2001-96871	20010914
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US 6638926	B2	20031028		
US 2003064981	A1	20030403	US 2001-952836	20010914
US 6613776	B2	20030902		
US 2003064982	A1	20030403	US 2001-952875	20010914
US 2003073687	A1	20030417	US 2001-952671	20010914
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US 2003083327	A1	20030501	US 2001-952833	20010914
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ES 2242771	T3	20051116	ES 2001-1971006	20010914
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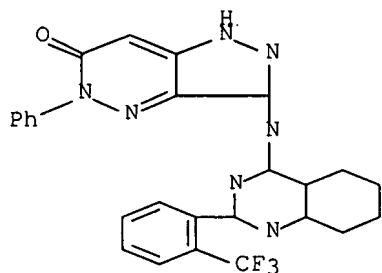
AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; Rx and Ry = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR<sub>6</sub>; or C<sub>2</sub>R<sub>2</sub>R<sub>2a</sub> = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>OCONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R<sub>3</sub> = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SOO-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R<sub>4</sub> = R<sub>7</sub>, COR<sub>7</sub>, CO<sub>2</sub>(aliphatic), CON(R<sub>7</sub>)<sub>2</sub>, or SO<sub>2</sub>R<sub>7</sub>; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>6</sub> and R<sub>7</sub> = independently H or (un)substituted aliphatic group; or N(R<sub>6</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; or N(R<sub>7</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>9</sub> = R, halo, OR, COR, CO<sub>2</sub>R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 = CR<sub>9</sub>; Z2 and Z3 = N; Z4 = CR<sub>y</sub>]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β<sub>3</sub>, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3β) and 0.1-1.0 μM for Aurora-2.

IT **404827-31-2P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-(2-trifluoromethylphenyl)quinazolin-4-yl)amine  
**404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
**404829-17-0P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine **404829-18-1P**, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-19-2P**, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-21-6P**, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-22-7P**, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-23-8P**, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

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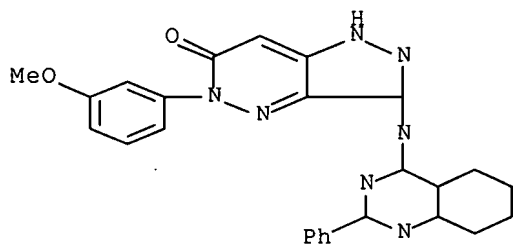
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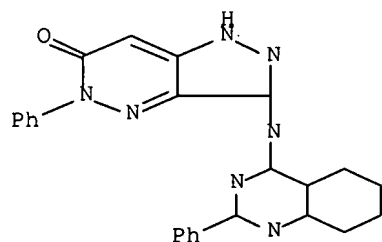
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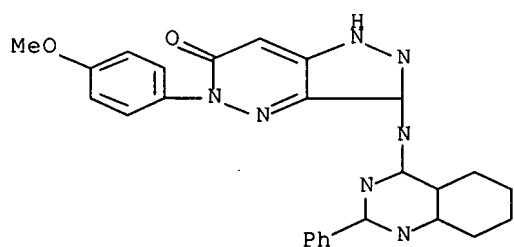
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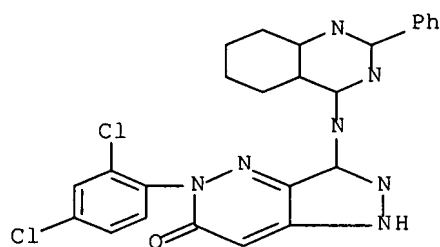
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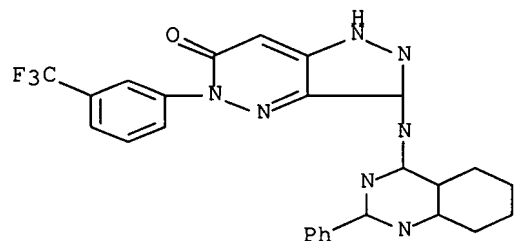
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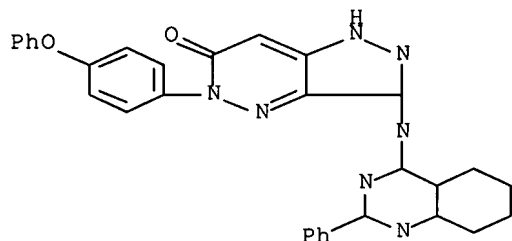


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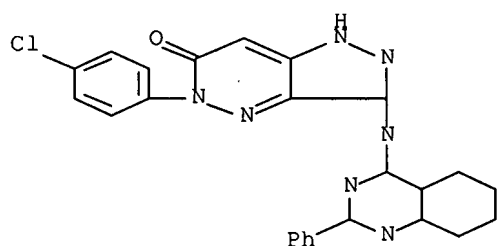




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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 7 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:220581 ZCAPLUS Full-text

DOCUMENT NUMBER: 136:247581

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Golec, Julian M. C.; Charrier, Jean-Damien; Knegt, Ronald; Bebbington, David; Davies, Robert; Li, Pan

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

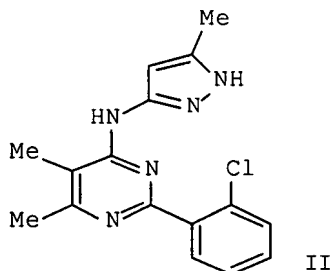
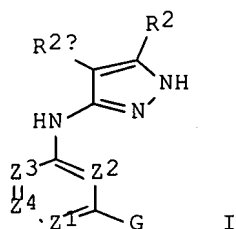
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OTHER SOURCE(S):  
GI

MARPAT 136:247581



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; Rx and Ry = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR<sub>6</sub>; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)2O, C(R<sub>6</sub>)2SO-2, C(R<sub>6</sub>)2NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>CONR<sub>6</sub>, C(R<sub>6</sub>)2NR<sub>6</sub>CO, C(R<sub>6</sub>)2NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)2NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)2NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)2NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SO<sub>2</sub>-2R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R4 = R7, COR7, CO<sub>2</sub>(aliphatic), CON(R7)<sub>2</sub>, or SO<sub>2</sub>R7; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R<sub>6</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; or N(R<sub>7</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO<sub>2</sub>R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrazolamines and indazolamines I [wherein Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N; at least one of Z1 or Z3 = N]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3β) and 0.1-1.0 μM for Aurora-2.

IT **404827-31-2P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine  
**404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
**404829-17-0P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine **404829-18-1P**, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-19-2P**, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-21-6P**, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-

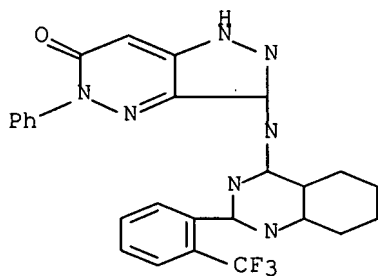
phenylquinazolin-4-yl)amine **404829-22-7P**, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl] (2-phenylquinazolin-4-yl)amine **404829-23-8P**, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl] (2-phenylquinazolin-4-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 ZCAPLUS

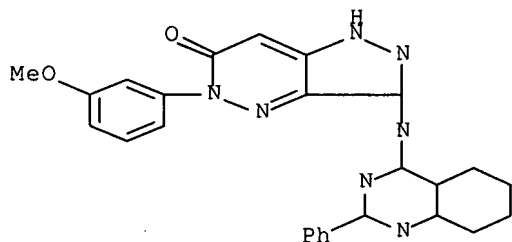
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 ZCAPLUS

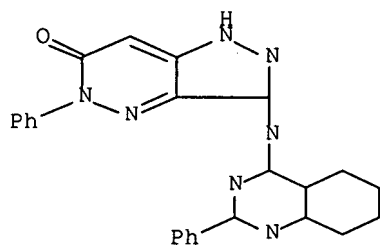
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 ZCAPLUS

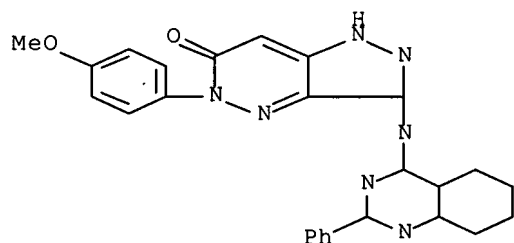
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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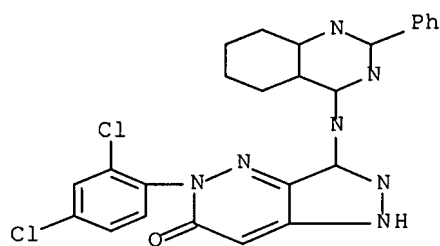
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 ZCAPLUS

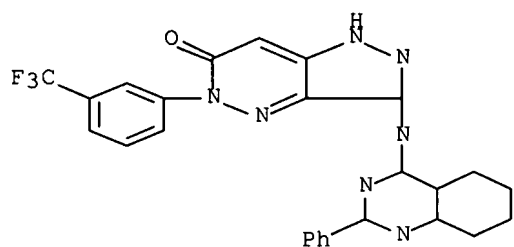
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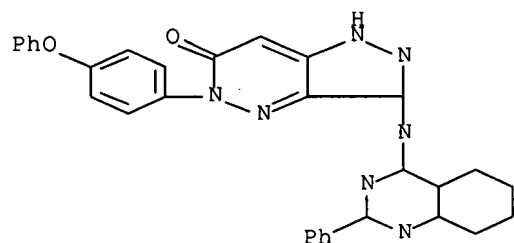
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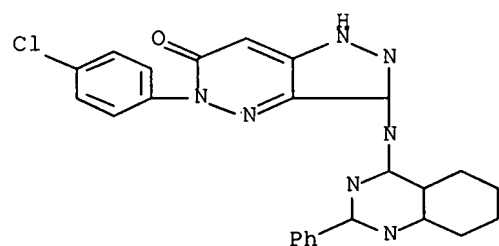
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 8 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:220579 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:247580

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Davies, Robert; Li, Pan; Golec, Julian; Bebbington, David  
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
SOURCE: PCT Int. Appl., 406 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 14  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022603	A1	20020321	WO 2001-US28738	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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US 6613776	B2	20030902		
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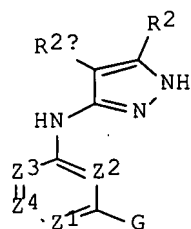


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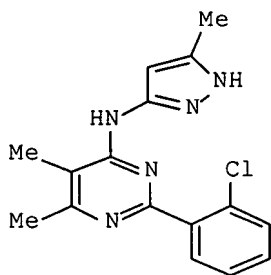
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WO 2001-US50312	W 20011219
US 2001-34019	A3 20011220
US 2001-34683	A1 20011220

OTHER SOURCE(S):  
GI

MARPAT 136:247580



I



II

AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6CONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (triazinyl)pyrazolamines and indazolamines I [wherein Z1, Z2, and Z3 = N; Z4 =

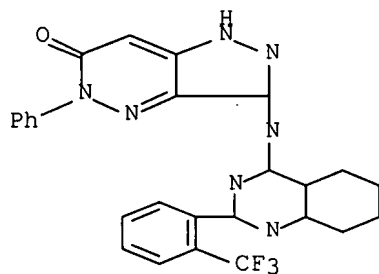
CRy]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- $\beta$ 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited  $K_i$  values of  $< 0.1 \mu\text{M}$  for glycogen synthetase kinase 3 $\beta$  (GSK-3 $\beta$ ) and  $0.1\text{--}1.0 \mu\text{M}$  for Aurora-2.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine  
 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 ZCAPLUS

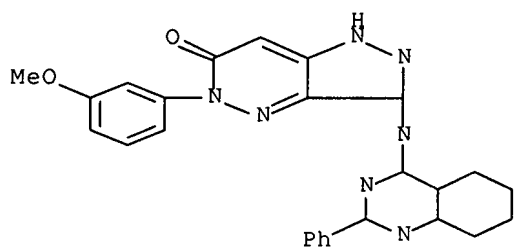
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-(2-(trifluoromethyl)phenyl]-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



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RN 404829-16-9 ZCAPLUS

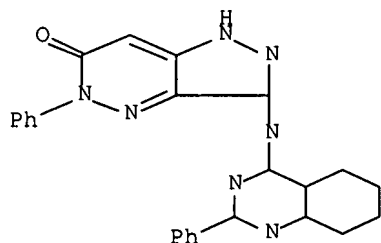
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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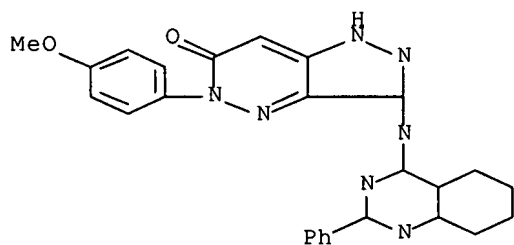
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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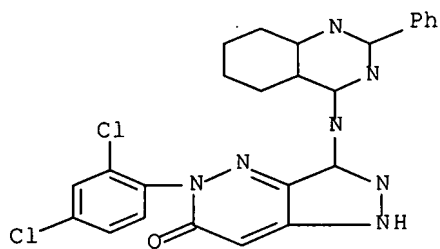
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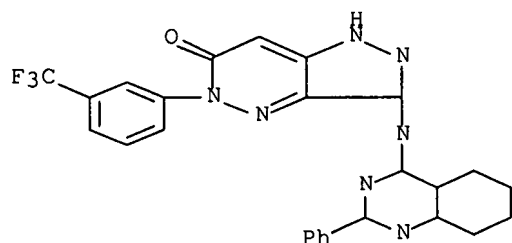
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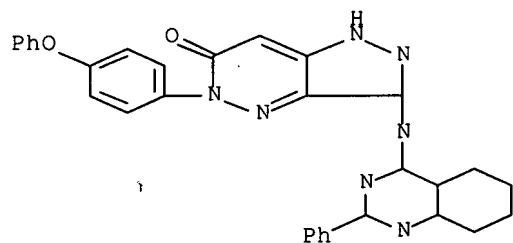
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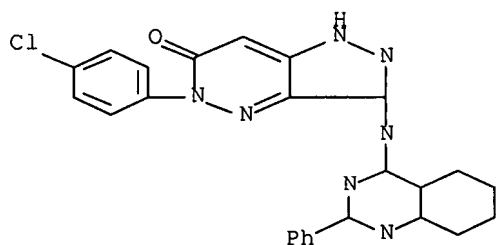
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE  
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 9 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:220578 ZCAPLUS Full-text  
DOCUMENT NUMBER: 136:263164  
TITLE: Preparation of triazolamines as protein kinase  
inhibitors for treatment of cancer, diabetes, and  
Alzheimer's disease  
INVENTOR(S): Bebbington, David; Knegetel, Ronald; Binch, Haley;  
Golec, Julian M. C.; Li, Pan; Charrier, Jean-Damien  
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA  
SOURCE: PCT Int. Appl., 377 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 14  
PATENT INFORMATION:

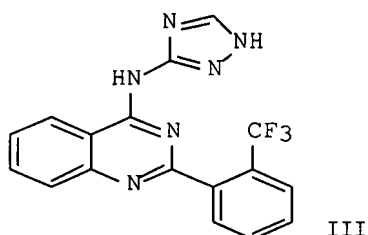
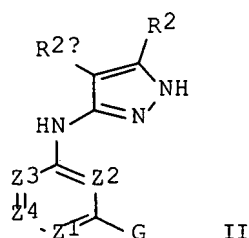
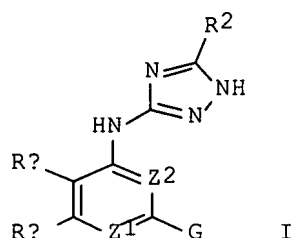
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OTHER SOURCE(S): MARPAT 136:263164  
GI





AB Triazolamines I and pyrazolamines II [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR<sub>9</sub>; Z2 = N or CH; Z3 = N or CR<sub>x</sub>; Z4 = N or CR<sub>y</sub>; R<sub>x</sub> and R<sub>y</sub> = independently TR<sub>3</sub>, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R<sub>2</sub> and R<sub>2a</sub> = independently R, TWR<sub>6</sub>; or C<sub>2</sub>R<sub>2</sub>R<sub>2a</sub> = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R<sub>6</sub>)<sub>2</sub>O, C(R<sub>6</sub>)<sub>2</sub>SO-2, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>, CO, CO<sub>2</sub>, CR<sub>6</sub>OCO, CR<sub>6</sub>OCONR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CO<sub>2</sub>, CR<sub>6</sub>:NNR<sub>6</sub>, CR<sub>6</sub>:NO, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>SO<sub>2</sub>NR<sub>6</sub>, C(R<sub>6</sub>)<sub>2</sub>NR<sub>6</sub>CONR<sub>6</sub>, or CONR<sub>6</sub>; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R<sub>3</sub> = R, halo, O, OR, COR, CO<sub>2</sub>R, COCOR, COCH<sub>2</sub>COR, NO<sub>2</sub>, CN, SO<sub>0-2</sub>R, N(R<sub>4</sub>)<sub>2</sub>, CON(R<sub>4</sub>)<sub>2</sub>, SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, OCOR, NR<sub>4</sub>COR, NR<sub>4</sub>CO<sub>2</sub>(aliphatic), NR<sub>4</sub>N(R<sub>4</sub>)<sub>2</sub>, C:NN(R<sub>4</sub>)<sub>2</sub>, C:NOR, NR<sub>4</sub>CO(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>N(R<sub>4</sub>)<sub>2</sub>, NR<sub>4</sub>SO<sub>2</sub>R, or OCON(R<sub>4</sub>)<sub>2</sub>; R<sub>4</sub> = R<sub>7</sub>, COR<sub>7</sub>, CO<sub>2</sub>(aliphatic), CON(R<sub>7</sub>)<sub>2</sub>, or SO<sub>2</sub>R<sub>7</sub>; or N(R<sub>4</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>6</sub> and R<sub>7</sub> = independently H or (un)substituted aliphatic group; or N(R<sub>6</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; or N(R<sub>7</sub>)<sub>2</sub> = heterocyclyl or heteroaryl; R<sub>9</sub> = R, halo, OR, COR, CO<sub>2</sub>R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (heterocyclyl)triazolamines I [wherein Z1 = N or CR<sub>9</sub>; Z2 = N or CH; R<sub>9</sub> is defined above]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β3, Aurora-2, ERK, and Src. For instance, the N-(4-quinazolinyl)-1H-1,2,4-triazol-3-amine III was prepared and exhibited K<sub>i</sub> values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3β) and 1.0-20 μM for Aurora-2.

IT **404827-31-2P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine  
**404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine  
**404829-17-0P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine **404829-18-1P**, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-19-2P**, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-21-6P**, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-

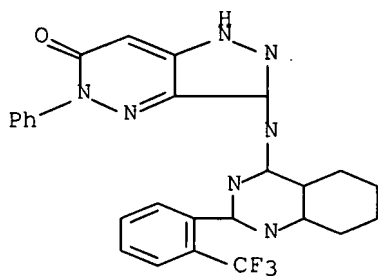
phenylquinazolin-4-yl)amine **404829-22-7P**, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-23-8P**, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 ZCAPLUS

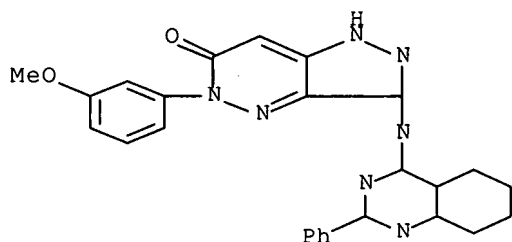
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 ZCAPLUS

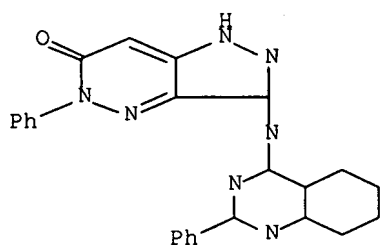
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 ZCAPLUS

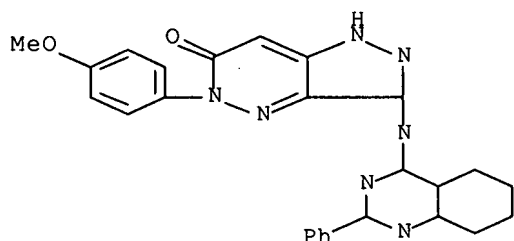
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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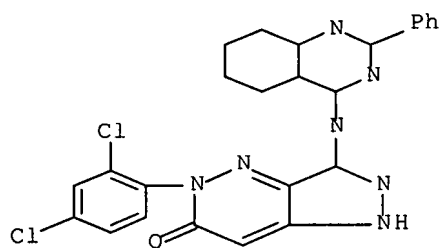
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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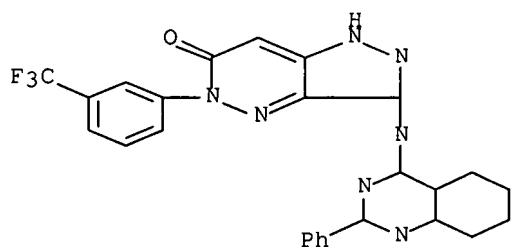
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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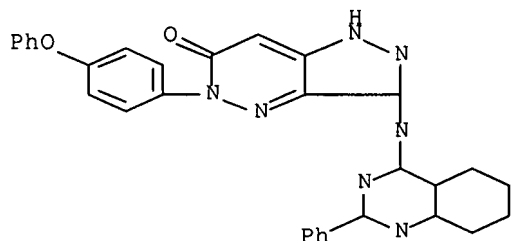
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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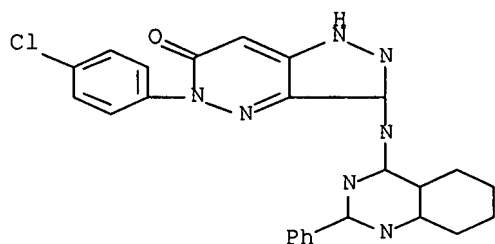
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L37 ANSWER 10 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:222320 ZCAPLUS Full-text

DOCUMENT NUMBER: 138:4553

TITLE: Synthesis and antimicrobial activity of some 5-pyrazolone derivatives

AUTHOR(S): Salman, A. S. S.

CORPORATE SOURCE: Department of Chemistry, Faculty of Science, Girl's Branch, Al- Azhar University, Nasr City, Egypt

SOURCE: Al-Azhar Journal of Pharmaceutical Sciences (2001),  
28, 48-62  
CODEN: AAJPFT; ISSN: 1110-1644  
PUBLISHER: Al-Azhar University, Faculty of Pharmacy  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 138:4553  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

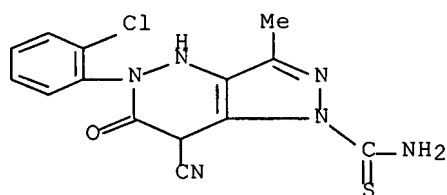
AB Reaction of pyrazolone I (R = H) with  $\beta$ -(p-phenylbenzoyl)acrylic acid and acrylonitrile afforded propionic acid derivative and (cyanoethyl)pyrazolone derivative resp. Condensation of thionocarbamoylpyrazolone I [R = CSNH<sub>2</sub> (II)] with anthranilic acid and Et cyanoacetate produced quinazolinone III and pyridazine derivs. Treatment of III with p-toluenesulfonyl chloride, phenylisothiocyanate, acrylonitrile and acetic anhydride yielded 3-substituted quinazolinones. Reaction of pyrazolone II with chloroacetic acid afforded thiazolinone IV. The structures of the new compds. were confirmed by elemental analyses, spectroscopic measurements, and chemical reactions. Some of the newly synthesized compds. showed interesting antibacterial activities in vitro.

IT 477283-22-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and antimicrobial activity of pyrazolones via cyclocondensation of (chlorophenyl)hydrazonoacetoacetate with hydrazine and semicarbazide followed by modifications of N-substituents)

RN 477283-22-0 ZCAPLUS

CN 1H-Pyrazolo[4,3-c]pyridazine-1-carbothioamide, 5-(2-chlorophenyl)-7-cyano-4,5,6,7-tetrahydro-3-methyl-6-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 11 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1993:482777 ZCAPLUS Full-text

DOCUMENT NUMBER: 119:82777

TITLE: Preparation of photographic cyan couplers

INVENTOR(S): Ikesu, Satoru; Kita, Hiroshi; Kaneko, Yutaka

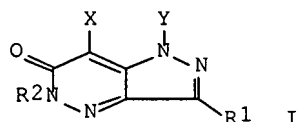
PATENT ASSIGNEE(S): Konica Co., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04307542	A	19921029	JP 1991-97860	19910404
PRIORITY APPLN. INFO.: GI			JP 1991-97860	19910404



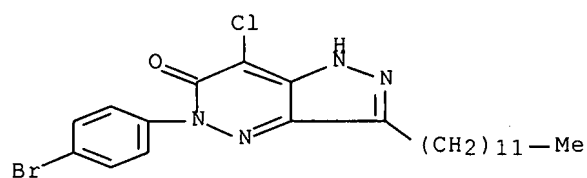
AB Pyrazolopyridazine derivs. (I; R1, R2, Y = H, substituent; X = H, substituent leaving upon reaction with the oxidized form of a color developing agent) are prepared I showed excellent stability against heat, humidity, and light.

IT 148665-07-0 148665-08-1 148665-09-2  
 148665-10-5 148665-11-6 148665-12-7  
 148665-13-8 148665-14-9 148665-15-0  
 148665-16-1 148665-17-2 148665-18-3  
 148665-19-4 148665-20-7 148665-21-8  
 148665-22-9 148894-29-5 148914-53-8

RL: TEM (Technical or engineered material use); USES (Uses)  
 (photog. cyan coupler)

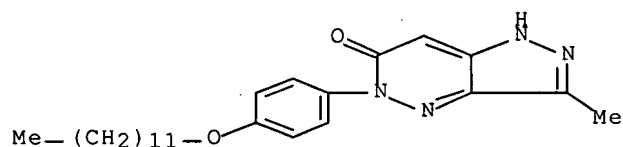
RN 148665-07-0 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-bromophenyl)-7-chloro-3-dodecyl-1,5-dihydro- (9CI) (CA INDEX NAME)



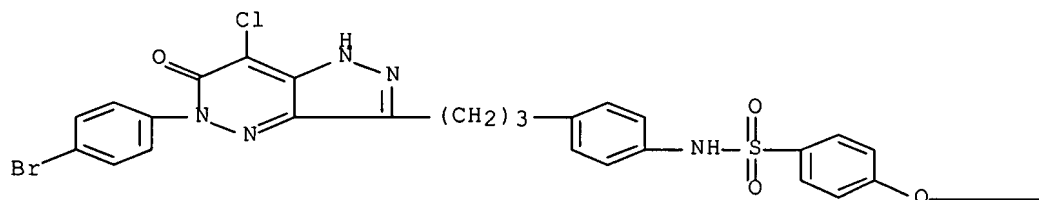
RN 148665-08-1 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[4-(dodecyloxy)phenyl]-1,5-dihydro-3-methyl- (9CI) (CA INDEX NAME)



RN 148665-09-2 ZCAPLUS  
 CN Benzenesulfonamide, N-[4-[3-[5-(4-bromophenyl)-7-chloro-5,6-dihydro-6-oxo-1H-pyrazolo[4,3-c]pyridazin-3-yl]propyl]phenyl]-4-(dodecyloxy)- (9CI) (CA INDEX NAME)

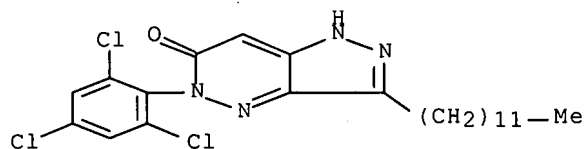
PAGE 1-A



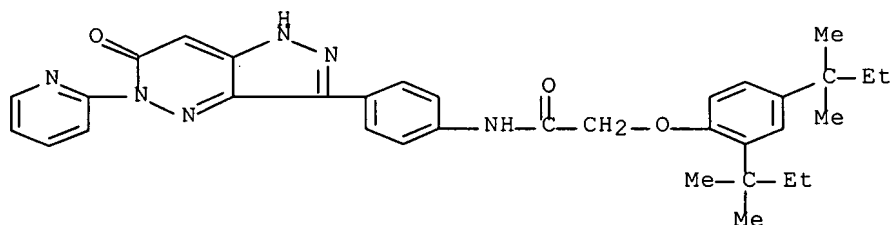
PAGE 1-B

— (CH<sub>2</sub>)<sub>11</sub>—Me

RN 148665-10-5 ZCAPLUS  
 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-dodecyl-1,5-dihydro-5-(2,4,6-trichlorophenyl)- (9CI) (CA INDEX NAME)

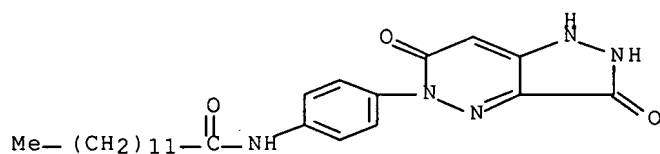


RN 148665-11-6 ZCAPLUS  
 CN Acetamide, 2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-N-[4-[5,6-dihydro-6-oxo-5-(2-pyridinyl)-1H-pyrazolo[4,3-c]pyridazin-3-yl]phenyl]- (9CI) (CA INDEX NAME)



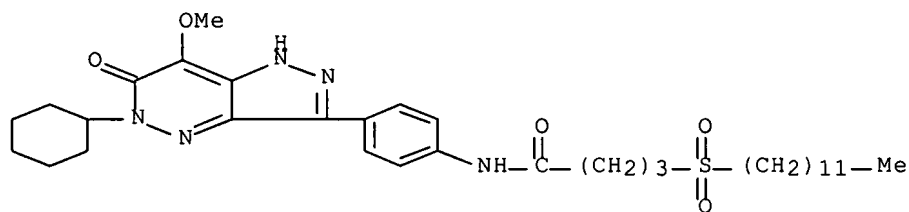
RN 148665-12-7 ZCAPLUS

CN Tridecanamide, N-[4-(1,2,3,6-tetrahydro-3,6-dioxo-5H-pyrazolo[4,3-c]pyridazin-5-yl)phenyl]- (9CI) (CA INDEX NAME)



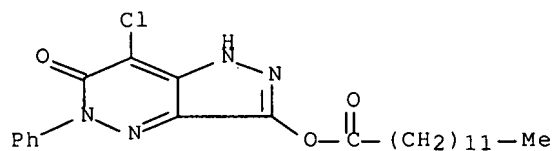
RN 148665-13-8 ZCAPLUS

CN Butanamide, N-[4-(5-cyclohexyl-5,6-dihydro-7-methoxy-6-oxo-1H-pyrazolo[4,3-c]pyridazin-3-yl)phenyl]-4-(dodecylsulfonyl)- (9CI) (CA INDEX NAME)



RN 148665-14-9 ZCAPLUS

CN Tridecanoic acid, 7-chloro-5,6-dihydro-6-oxo-5-phenyl-1H-pyrazolo[4,3-c]pyridazin-3-yl ester (9CI) (CA INDEX NAME)

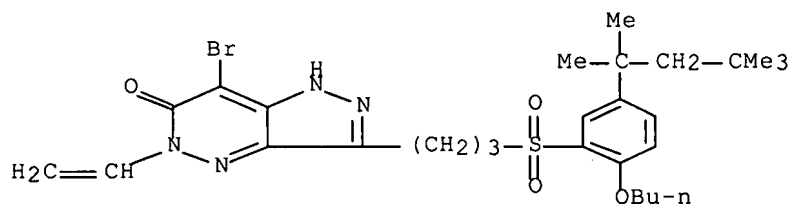


RN 148665-15-0 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 7-bromo-3-[3-[[2-butoxy-5-(1,1,3,3-

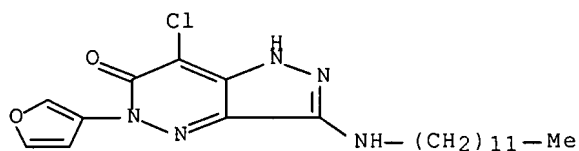


tetramethylbutyl]phenyl]sulfonyl]propyl]-5-ethenyl-1,5-dihydro- (9CI) (CA INDEX NAME)



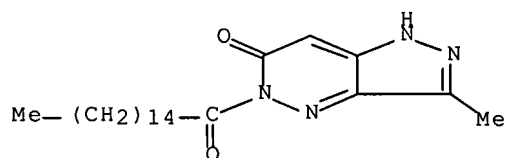
RN 148665-16-1 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 7-chloro-3-(dodecylamino)-5-(3-furanyl)-1,5-dihydro- (9CI) (CA INDEX NAME)



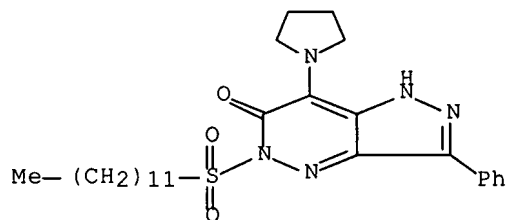
RN 148665-17-2 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-methyl-5-(1-oxohexadecyl)- (9CI) (CA INDEX NAME)

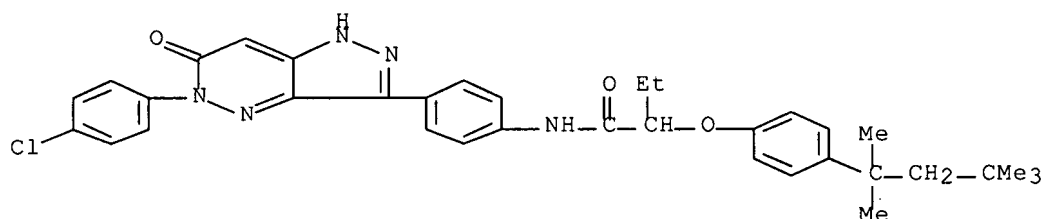


RN 148665-18-3 ZCAPLUS

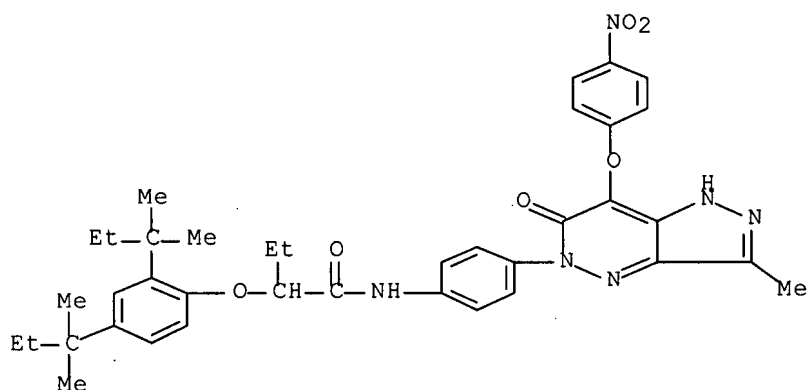
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(dodecylsulfonyl)-1,5-dihydro-3-phenyl-7-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



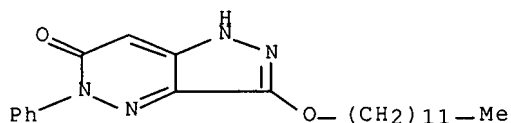
RN 148665-19-4 ZCAPLUS  
 CN Butanamide, N-[4-[5-(4-chlorophenyl)-5,6-dihydro-6-oxo-1H-pyrazolo[4,3-c]pyridazin-3-yl]phenyl]-2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]- (9CI)  
 (CA INDEX NAME)



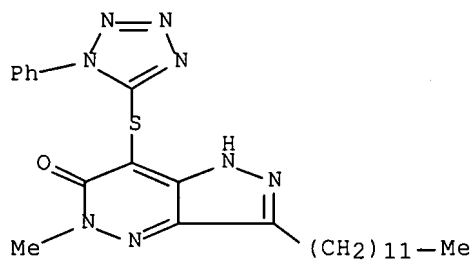
RN 148665-20-7 ZCAPLUS  
 CN Butanamide, 2-[2,4-bis(1,1-dimethylpropyl)phenoxy]-N-[4-[1,6-dihydro-3-methyl-7-(4-nitrophenoxy)-6-oxo-5H-pyrazolo[4,3-c]pyridazin-5-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 148665-21-8 ZCAPLUS  
 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-(dodecyloxy)-1,5-dihydro-5-phenyl- (9CI) (CA INDEX NAME)

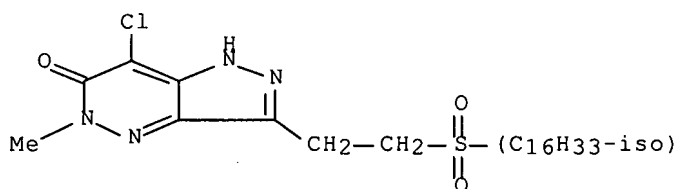


RN 148665-22-9 ZCAPLUS  
 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 3-dodecyl-1,5-dihydro-5-methyl-7-[(1-phenyl-1H-tetrazol-5-yl)thio]- (9CI) (CA INDEX NAME)



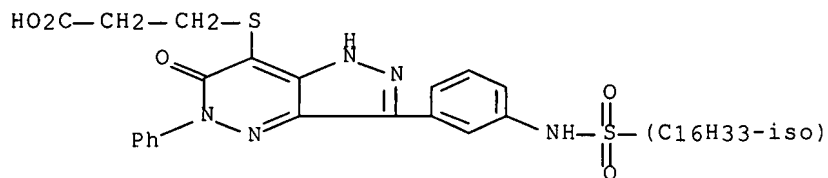
RN 148894-29-5 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 7-chloro-1,5-dihydro-3-[2-(isohexadecylsulfonyl)ethyl]-5-methyl- (9CI) (CA INDEX NAME)



RN 148914-53-8 ZCAPLUS

CN Propanoic acid, 3-[[5,6-dihydro-3-[3-[(isohexadecylsulfonyl)amino]phenyl]-6-oxo-5-phenyl-1H-pyrazolo[4,3-c]pyridazin-7-yl]thio]- (9CI) (CA INDEX NAME)

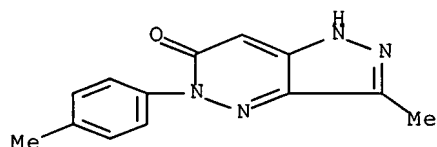


IT 148665-06-9P

RL: PREP (Preparation)  
(preparation of, as photog. cyan coupler)

RN 148665-06-9 ZCAPLUS

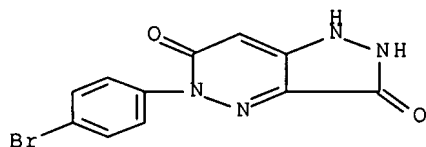
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-methyl-5-(4-methylphenyl)- (9CI) (CA INDEX NAME)



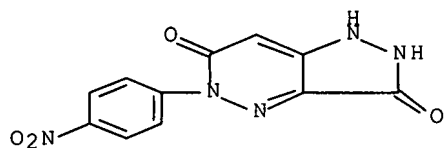
L37 ANSWER 12 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 1990:198276 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 112:198276  
 TITLE: Synthesis and biological activity of substituted  
 1,4,5,6-tetrahydropyridazin-4-ones,  
 5,6-dihydro-3-hydroxy-1H-pyrazolo[4,3-c]pyridazines  
 and 2,8-dihydro-1H-pyrano[2,3-d]pyridazines  
 AUTHOR(S): Patel, Himatkumar V.; Fernandes, P. S.  
 CORPORATE SOURCE: Dep. Chem., St. Xavier's Coll., Bombay, 400 001, India  
 SOURCE: Indian Journal of Chemistry, Section B: Organic  
 Chemistry Including Medicinal Chemistry (1989),  
 28B(9), 733-44  
 CODEN: IJSBDB; ISSN: 0376-4699  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 112:198276  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

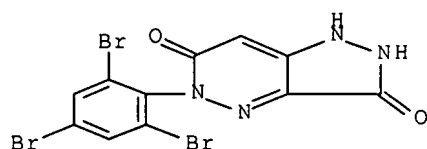
AB The preparation of title compds., e.g. I, II and III, from  $RNHN=C(COMe)CO_2Et$   
 (R = Ph, 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, 4-BrC<sub>6</sub>H<sub>4</sub>, 2,4,6-Br<sub>3</sub>C<sub>6</sub>H<sub>2</sub>) is reported. A number of these  
 compds. including II and III showed bactericidal activity.  
 IT **126837-11-4P 126837-55-6P 126837-56-7P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
 study); PREP (Preparation)  
 (preparation and bactericidal activity of)  
 RN 126837-11-4 ZCAPLUS  
 CN 1H-Pyrazolo[4,3-c]pyridazine-3,6(2H,5H)-dione, 5-(4-bromophenyl)- (9CI)  
 (CA INDEX NAME)



RN 126837-55-6 ZCAPLUS  
 CN 1H-Pyrazolo[4,3-c]pyridazine-3,6(2H,5H)-dione, 5-(4-nitrophenyl)- (9CI)  
 (CA INDEX NAME)



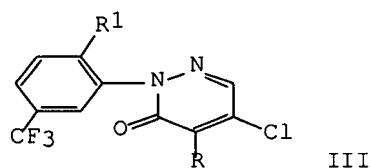
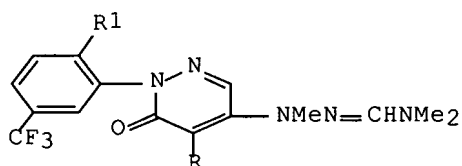
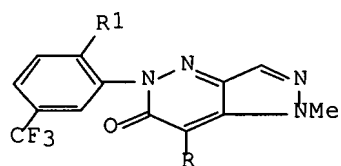
RN 126837-56-7 ZCAPLUS  
 CN 1H-Pyrazolo[4,3-c]pyridazine-3,6(2H,5H)-dione, 5-(2,4,6-tribromophenyl)-  
 (9CI) (CA INDEX NAME)



L37 ANSWER 13 OF 40 ZCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 1977:171486 ZCAPLUS Full-text  
 DOCUMENT NUMBER: 86:171486  
 TITLE: Antihypertensive aryl pyrazolo[4,3-c]pyridazinones  
 INVENTOR(S): Anderson, Paul L.  
 PATENT ASSIGNEE(S): Sandoz-Wander, Inc., USA  
 SOURCE: U.S., 5 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 4004009	A	19770118	US 1975-600885	19750731
PRIORITY APPLN. INFO.:			US 1975-600885	A 19750731

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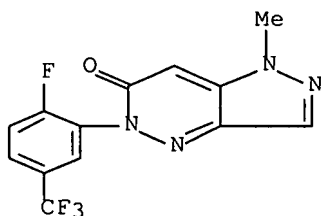
AB Antihypertensive pyrazolopyridazinones I (R = H, Cl; R1 = H, F) were obtained together with hydrazinopyridazinones II by treating the chloropyridazinones III with MeNHNH2 and Me2NCH(OMe)2.

IT 62529-56-0P 62529-58-2P 62529-60-6P  
62529-61-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

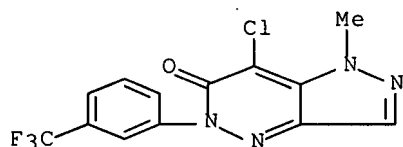
RN 62529-56-0 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-[2-fluoro-5-(trifluoromethyl)phenyl]-1,5-dihydro-1-methyl- (9CI) (CA INDEX NAME)



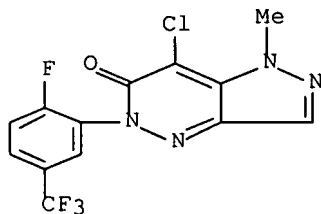
RN 62529-58-2 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 7-chloro-1,5-dihydro-1-methyl-5-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 62529-60-6 ZCAPLUS

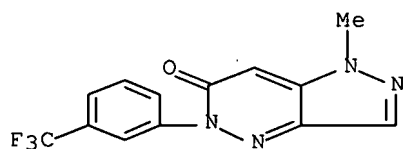
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 7-chloro-5-[2-fluoro-5-(trifluoromethyl)phenyl]-1,5-dihydro-1-methyl- (9CI) (CA INDEX NAME)



RN 62529-61-7 ZCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-1-methyl-5-[3-

(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



L37 ANSWER 40 OF 40 BABS COPYRIGHT 2007 BEILSTEIN MDL on STN

ACCESSION NUMBER: 5574813 BABS Full-text

TITLE: Synthesis and biological activity of substituted  
1,4,5,6-tetrahydropyridazin-4-ones,  
5,6-dihydro-3-hydroxy-1H-pyrazolo<4.3-c>pyridazines  
and 2,8-dihydro-1H-pyrano<2,3-d>pyridazines

AUTHOR(S): Patel, Himatkumar V.; Fernandes, P. S.

SOURCE: Indian J.Chem.Sect.B (1989), 28(1-11), 733-744

CODEN: IJSBDB

DOCUMENT TYPE: Journal

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Ethyl arylazoacetoacetates (1) when reacted with benzaldehyde in the presence of a base give the corresponding ethyl 2,3-dioxo-5-phenylpent-4-enoate 2-arylhydrazones (2), which are transformed into 1,4,5,6-tetrahydro-1-aryl-3-carbethoxy-6-phenylpyridazin-4-ones (3). Compounds 1 are converted into ethyl arylazo-\$g\$-bromoacetoacetates (10) which react with KCN in DMF to yield the corresponding ethyl 1,4,5,6-tetrahydro-1-aryl-6-imino-4-oxo-3-pyridazinecarboxylates (12). The compound 12 on reaction with acetic anhydride give O,N-diacetyl derivatives (13), while with benzoylchloride in pyridine they afford O,N-dibenzoyl derivatives (14). Nitrosation of 12 affords N-nitroso derivatives (15) which are decomposed by heating with xylene to give the corresponding ethyl 1,4,5,6-tetrahydro-1-aryl-

(16).The compounds 4,6-dioxo-3-pyridazinecarboxylates  
 12 and 16 on treatment with  
 hydrazine hydrate in the  
 presence of catalytic amount of HCl  
 yield the  
 corresponding 5,6-dihydro-3-hydroxy-  
 1H-pyrazolo<4.3-  
 d>pyridazines (17 and 18).Compounds  
 3, 12 and 16 on  
 reaction with a few activated  
 olefins such as  
 benzalacetophenone, benzalacetone,  
 3-benzylideneacetylacetone, diethyl  
 2-benzylidenemalonate and  $\alpha$ -cyano-  
 $\beta$ -phenylacrylic  
 acid in the presence of an organic  
 base like  
 pyrolidine, morpholine, piperidine  
 or triethylamine  
 give the corresponding substituted  
 2,8-dihydro-1H-pyrano<2,3-  
 d>pyridazines (5-9,  
 19-28).Structural assignments have  
 been made on the  
 basis of spectral data, elemental  
 analysis, chemical  
 behaviour and alternate synthesis  
 wherever  
 possible.Some of the compounds have  
 been tested for  
 their biological activity.

L37 ANSWER 14 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 146:421993 MARPAT Full-text  
 TITLE: Preparation of nitrogenated heterocyclic compounds as  
 xanthine oxidase inhibitors and pharmaceutical  
 compositions comprising the same  
 INVENTOR(S): Toyoshima, Takahiro; Sasaki, Toshinobu; Hoshino,  
 Chikara; Takeda, Masakazu  
 PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 64pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007043401	A1	20070419	WO 2006-JP319806	20061003
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

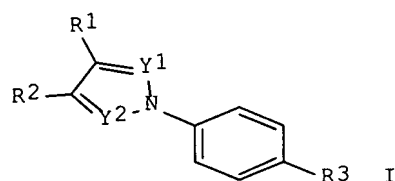


GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW  
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

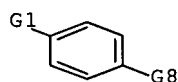
JP 2005-295429 20051007

GI

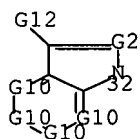


AB N-phenylazole heterocyclic compds. represented by the general formula (I) or pharmaceutically acceptable salts thereof [Y1 = N or C(R4); Y2 = N or C(R5); R4, R5 = H, alkyl, haloalkyl, cyano, alkoxy; one of R1 and R2 = (un)substituted aryl, alkoxy, or each (un)substituted thienyl, thiazolyl, or pyrrolyl; R3 = 5-tetrazolyl or CO2H] or pharmacol. acceptable salts thereof are prepared These compds. have a xanthine oxidase inhibitory activity and an uric acid excretion promoting activity and are useful for the treatment of gout, hyperuricemia, ischemic reperfusion disorder, inflammatory diseases, diabetes, cancer, arteriosclerosis, or neurotic disorder. Thus, condensation of acetophenone with 4-hydrazinobenzoic acid in aqueous acetic solution at 100° for 21 h gave 4-[N'-(1- phenylethylidene)hydrazino]benzoic acid which underwent esterification with MeOH in the presence of concentrated H2SO4 under refluxing for 30 h to give 4-[N'-(1-phenylethylidene)hydrazino]benzoic acid Me ester (II). Cyclization and formylation of II with POCl3 in DMF at room temperature for 12 h gave 4-(4-formyl-3-phenyl-1H-pyrazol-1-yl)benzoic acid Me ester which was refluxed with formic acid, sodium formate, and hydroxylamine hydrochloride to give 4-(4-cyano-3-phenyl-1H-pyrazol-1-yl)benzoic acid Me ester (III). Saponification of III with Na2CO3 in aqueous 1,4-dioxane at 80° followed by acidification with 2 M aqueous HCl solution gave 4-(4-cyano-3-phenyl-1H-pyrazol-1- yl)benzoic acid (IV). IV and 4-[4-cyano-3-(2-fluorophenyl)-1H-pyrazol-1- yl]benzoic acid showed IC50 of 8.18 and 2.91 nM against buttermilk xanthine oxidase.

MSTR 1



G1 = 32



G2 = N

G10 = (up to 1) N / 34

34—G11

G11 = alkoxy

Patent location: claim 1

Note: or pharmaceutically acceptable salts

Note: additional ring formation also claimed

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 15 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 146:441780 MARPAT Full-text

TITLE: Preparation of diacylindazoles as inhibitors of hormone-sensitive lipase (HSL) and endothelial lipase (EL)

INVENTOR(S): Zoller, Gerhard; Petry, Stefan; Mueller, Guenter; Heuer, Hubert; Tennagels, Norbert

PATENT ASSIGNEE(S): Sanofi-Aventis Deutschland GmbH, Germany

SOURCE: PCT Int. Appl., 75pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007042178	A1	20070419	WO 2006-EP9577	20061004

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

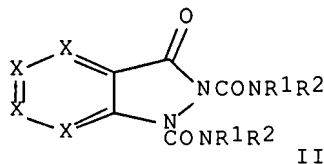
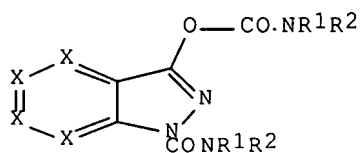
DE 102005048897 A1 20070419

DE 2005-10200504889720051012

PRIORITY APPLN. INFO.:

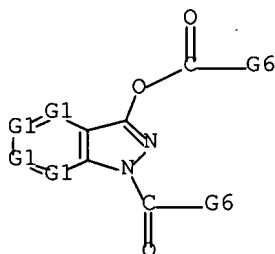
DE 2005-10200504889720051012

GI

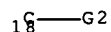


AB Title compds. [I, II; X = CR, N, wherein  $\leq 2$  X = N; R = H, halo, alkyl, alkoxyalkylene, haloalkyl, OH, alkylmercapto, amino, etc.; R1 = alkyl, cycloalkyl, etc.; R2 = H; or NR1R2 = (saturated) monocyclic 4-7 membered ring, bicyclic (saturated) 8-14 interrupted ring system], were prepared Thus, 3-oxo-1,3-dihydroindazole-2-carboxylic acid 2-methylbenzylamide (preparation given) in pyridine was stirred with Et3N and 4-methylpiperidine-1-carbonyl chloride for 7 h at room temperature followed by further treatment with 4-methylpiperidine-1-carbonyl chloride and Et3N and stirring for 7 h to give 66% 1-(4-methylpiperidine-1-carbonyl)-3-oxo-1,3-dihydroindazole-2-carboxylic acid 2-methylbenzylamide. The latter inhibited EL with IC50 = 0.22  $\mu$ M.

**MSTR 1**



G1 = (up to 2) N / 18



G2 = OH

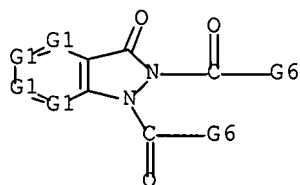
Patent location:

Note:

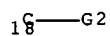
claim 1

and tautomeric forms and physiologically acceptable salts

**MSTR 2**



G1 = (up to 2) N / 18



G2 = OH

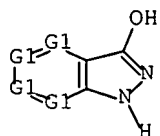
Patent location:

Note:

claim 1

and tautomeric forms and physiologically acceptable salts

*MSTR 3*



G1 = (up to 2) N / 18



G2 = OH

Patent location:

claim 18

REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 16 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 146:402148 MARPAT Full-text

TITLE: Preparation of azabicyclic derivs. of indazoles, benzothiazoles, benzoisothiazoles, benzisoxazoles, pyrazolopyridines, isothiazolopyridines for therapeutic use as  $\alpha 7$ -nACh receptor activators

INVENTOR(S): Schumacher, Richard; Danca, Mihaela Diana; Ma, Jianguo; Herbert, Brian; Nguyen, Truc Minh; Xie, Wenge; Tehim, Ashok

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA

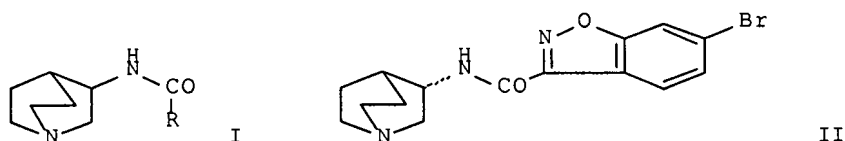
SOURCE: PCT Int. Appl., 283pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007038367	A1	20070405	WO 2006-US37142	20060922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007078147	A1	20070405	US 2006-525213	20060922
PRIORITY APPLN. INFO.:			US 2005-719552P	20050923
			US 2006-791881P	20060414

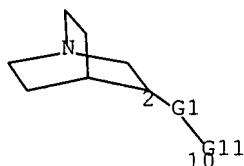
GI



AB N-azabicyclo[2.2.2]octyl-heterocyclic amide derivs., such as I [R = heterocyclyl, such as those cited in the title], were prepared as  $\alpha 7$  nicotinic acetylcholine receptor ( $\alpha 7$ -nAChR) ligands which activate or enhance defective or malfunctioning nAChR activity, especially of the brain, and are useful in the treatment of psychotic disease, neurodegenerative disease and conditions of memory and/or cognition impairment. These diseases and conditions may include schizophrenia, anxiety, mania, depression, manic depression, Tourette's syndrome, Parkinson's disease, Huntington's disease, Alzheimer's disease, Lewy body dementia, amyotrophic lateral sclerosis, memory impairment, memory loss, cognition deficit, attention deficit, attention deficit hyperactivity disorder (ADHD) and mild cognitive impairment due to aging, Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, depression, aging, head trauma, stroke, CNS hypoxia, cerebral senility, multiinfarct dementia, HIV and/or cardiovascular disease. These diseases may further include alc. and nicotine addiction, pain, jet lag, obesity, diabetes, vascular dementia (VaD), age-associated cognitive decline (AACD), amnesia associated with open-heart-surgery, cardiac arrest, general anesthesia, memory deficits from exposure to anesthetic agents, sleep deprivation induced cognitive impairment, chronic fatigue syndrome, narcolepsy, AIDS-related dementia, epilepsy-related cognitive impairment, Down's syndrome, alcoholism related dementia, drug/substance induced memory impairments and dementia puglistica (boxer

syndrome). Thus, amide II was prepared via an amidation reaction of (3S)-3-aminoquinuclidine hydrochloride with Et 6-bromobenzisoxazole-3-carboxylate in EtOH using N,N- diisopropylethylamine. The prepared amides were assayed for  $\alpha 7$ -nAChR binding affinity.

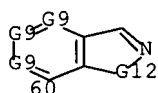
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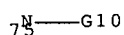
G9 = N / 161



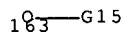
G11 = 60



G12 = 75



G14 = 163



Patent location:  
Note:

claim 1  
and pharmaceutically acceptable salts, solvates,  
N-oxides, or solvates of pharmaceutically  
acceptable salts, or pharmaceutically acceptable  
salts or solvates of N-oxides, or polymorphs  
additional ring formation also claimed  
and stereoisomers

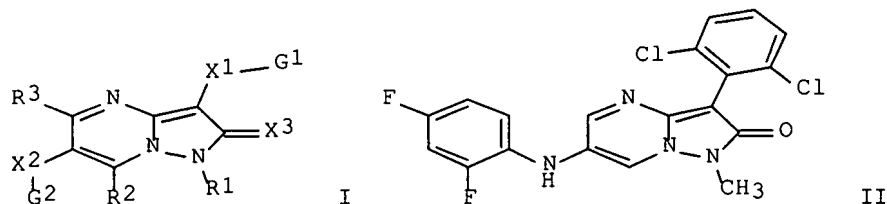
Note:  
Note:

ACCESSION NUMBER: 146:229369 MARPAT Full-text  
 TITLE: Preparation of pyrazolo[1,5-a]pyrimidinones as p38 kinase inhibitors for the treatment of inflammatory disorders  
 INVENTOR(S): Severance, Daniel L.; Borchardt, Allen J.; Gardiner, Elisabeth M. M.; Kahraman, Mehmet  
 PATENT ASSIGNEE(S): Kalypsys, Inc., USA  
 SOURCE: PCT Int. Appl., 95pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007015866	A2	20070208	WO 2006-US27863	20060718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:  
 US 2005-701183P 20050720  
 US 2005-701217P 20050720  
 US 2005-701250P 20050720  
 US 2005-701251P 20050720  
 US 2005-701253P 20050720  
 US 2005-701254P 20050720  
 US 2006-780186P 20060308  
 US 2006-790189P 20060407

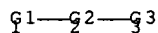
GI



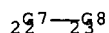
AB Pyrazolo[1,5-a]pyrimidinones and their analogs, such as I [wherein X1, X2 = bond, O, S, etc.; G1, G2 = (un)substituted (hetero)aryl, cycloalkyl or heterocyclyl; X3 = O or S; R1 - R3 = H, alkyl, aryl, etc.], and pharmaceutically acceptable salts, esters, or prodrugs thereof were prepared as p38 kinase inhibitors. For instance, II was synthesized in multiple steps.

This compound showed inhibition of p38 $\alpha$  kinase with IC<sub>50</sub>  $\leq$  1  $\mu$ M, and had IC<sub>50</sub>  $\leq$  1  $\mu$ M in a TNF $\alpha$  ELISA cellular assay. Therefore, the invented compds. and their pharmaceutical compns. are useful for the treatment of p38 kinase-mediated diseases, such as inflammation.

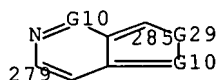
# MSTR 1B



G1 = 22



G2 = 279-1 285-3



G7 = O

G10 = N

G29 = NH

Patent location:

claim 1

Note:

or pharmaceutically acceptable salts, esters, or prodrugs

Note:

additional substitution also claimed

Note:

also incorporates later claims and broader disclosure

L37 ANSWER 18 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 146:121980 MARPAT Full-text

TITLE: Preparation of azaindazole compounds as CCR1 antagonists

INVENTOR(S): Zhang, Penglie; Pennell, Andrew M. K.; Wright, John J. Kim; Chen, Wei; Leleti, Manmohan R.; Li, Yandong; Li, Lianfa; Xu, Yuan

PATENT ASSIGNEE(S): Chemocentryx, Inc., USA

SOURCE: PCT Int. Appl., 121pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007002293	A2	20070104	WO 2006-US24313	20060622



WO 2007002293 A3 20070308

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2007010523 A1 20070111

US 2006-474130 20060622

US 2007010524 A1 20070111

US 2006-474132 20060622

PRIORITY APPLN. INFO.:

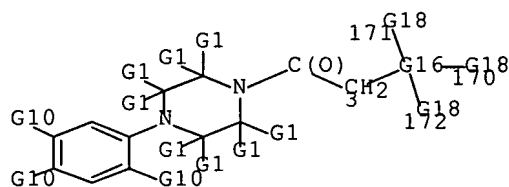
US 2005-693525P 20050622

GI

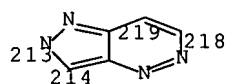
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I and II [R1 = alkyl, haloalkyl, cycloalkyl, etc.; R2a, R2c, R2d = H, halo, cyano, etc.; each of ring vertices a, b, c and d is selected from N and C(R3a), and from one to two of said ring vertices is N; R3a = H, halo, -ORf, etc.; Rf = H, alkyl, haloalkyl, etc.; m = 0-2], pharmaceutically acceptable salts, hydrates or N-oxides thereof were prepared For example, 2-chloro-1-[4-(4-chloro-2-fluoro-5-methoxyphenyl)-2- (S)-methylpiperazin-1-yl]ethanone (1 .0 equiv) was reacted with 1H-pyrazolo[3,4-b]pyridine (1.2 equiv) and K2CO3 (10.0 equiv) in DMF at 80° for 1h, then chromatographed to give compound III and IV. In CCR1 binding assays, each exemplified compound III and IV exhibited the IC50 value of <1000 nM. Compds. I are claimed useful for the treatment of rheumatoid arthritis, multiple sclerosis, etc.

# MSTR 1



G16 = 213-3 214-172 218-170 219-171



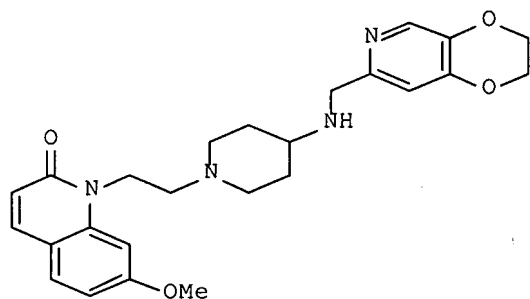
G18 = OH (opt. substd.)

Patent location: claim 1  
Note: additional derivatization also disclosed  
Note: or pharmaceutically acceptable salts, hydrates or N-oxides

L37 ANSWER 19 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 146:81779 MARPAT Full-text  
TITLE: Preparation of quinolinones and analogs for the treatment of multi-drug resistant bacterial infections  
INVENTOR(S): Breault, Gloria; Eyermann, Charles Joseph; Geng, Bolin; Morningstar, Marshall; Reck, Folkert  
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited  
SOURCE: PCT Int. Appl., 209pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006134378	A1	20061221	WO 2006-GB2207	20060616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2005-691340P 20050616  
GI

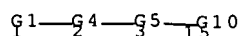


II

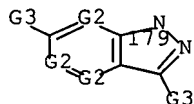
AB The invention is related to compds. L-U1-M-U2-R [I; L = (un)substituted 2-oxo-1,2-dihydroquinolin-1-yl, 2-oxo-1,4-dihydroquinolin-1-yl, 3-oxo-2,3-dihydro-4H-1,4-benzoxazin-4-yl, 2,4-dioxo-3,4-dihydroquinazolin-1(2H)-yl, 2-oxo-1,8-

naphthyridin-1(2H)-yl, 2-oxoquinoxalin-1(2H)-yl, 3-oxopyrido[2,3-b]pyrazin-4(3H)-yl, etc.; U1 = CRaRb-CRcRd, CRaRb-CRcRd-CReRf; Ra-f = independently H, (un)substituted alkyl; M = (un)substituted 1,4-piperidinylene, 1,4-pyrazinylene, 2,5-piperidinylene, etc.; U2 = NR'-W; R' = H, alkyl, alkylcarbonyl, etc.; W = CH2, CO, CO2, CH2CH2, etc.; when W = CH2, CO or SO2, R = (un)substituted hetero/aryl, heterocyclyl, or ortho-fused bicyclic heteroaryl; when W = CH2CH2, CH2CH:CH, CH2C.tplbond.C, or CH2-cyclopropylene, R = (un)substituted hetero/aryl, heteroaryloxy, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heteroarylamino; with proviso] their pharmaceutically acceptable salts, and N-oxides that demonstrate antibacterial activity, processes for their preparation, pharmaceutical compns. containing them as the active ingredient, to their use as medicaments and to their use in the manufacture of medicaments for use in the treatment of multi-drug resistant bacterial infections in warm blooded animals such as humans. Thus, alkylation of 7-methoxyquinolin-2(1H)-one with 2-[4-[(tert-butoxycarbonyl)amino]piperidin-1-yl]ethyl methanesulfonate, deprotection, and reduction amination of 2,3-dihydro-[1,4]dioxino[2,3-c]pyridine-7-carboxaldehyde with the amine intermediate gave oxoquinoline salt II•2HCl. Compds. I generally have IC50 <20 µg/mL for inhibition of Escherichia coli DNA supercoiling and GyrB ATPase activities and have MIC's ≤8 µg/mL vs. Gram-pos. species, including Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes, and Enterococcus faecium and vs. Gram-neg. species including Haemophilus influenzae, Escherichia coli and Moraxella catarrhalis.

#### MSTR 1



G1 = 179



G2 = N / CH (opt. substd.)

G3 = OH

Patent location:

claim 1

Note:

also incorporates a structure from claim 20

Note:

substitution is restricted

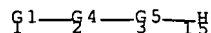
Note:

additional ring formation also claimed

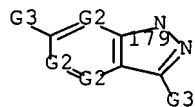
Note:

or pharmaceutically acceptable salts or N-oxides

#### MSTR 2



G1 = 179



G2 = N / CH (opt. substd.)

G3 = OH

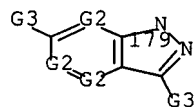
Patent location: claim 20

Note: additional ring formation also claimed

### MSTR 3

G1—G4

G1 = 179



G2 = N / CH (opt. substd.)

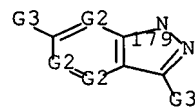
G3 = OH

Patent location: claim 20

### MSTR 5

G1—G4—G5—G10

G1 = 179



G2 = N / CH (opt. substd.)

G3 = OH

Patent location:

claim 20

Note:

additional ring formation also claimed

REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 20 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 145:124600 MARPAT Full-text

TITLE: Preparation of bicyclic heterocyclyl phenyl ketones as antitumor agents

INVENTOR(S): Hsieh, Hsing-Pang; Chao, Yu-Sheng; Liou, Jing-Ping; Chang, Jang-Yang; Tung, Yen-Shih

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 17 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006148801	A1	20060706	US 2005-300873	20051215
AU 2005322936	A1	20060713	AU 2005-322936	20051228
WO 2006074041	A2	20060713	WO 2005-US47366	20051228
WO 2006074041	A3	20061123		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

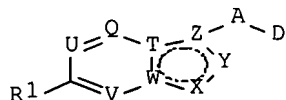
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

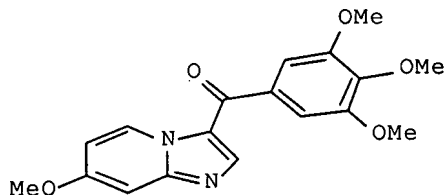
US 2004-641218P 20041231

WO 2005-US47366 20051228

GI



I

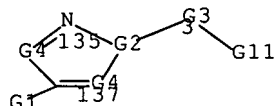


II

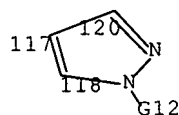
AB Title compds. I [wherein A = C(O); O, S, etc.; D = (hetero)aryl; R1 = H, alkyl, aryl, etc.; Q, U, V, Y = (un)substituted C or N; X = N, O, S, etc.; Z = C; T, W = C or N, with limitations] were prepared For instance, successive

formylation of 7-methoxyimidazo[1,2-a]pyridine with POCl<sub>3</sub>-DMF (69% yield), nucleophilic addition of a Grignard reagent generated in situ from 3,4,5-trimethoxybromobenzene, and oxidation of the resulting alc. with MnO<sub>2</sub> (76% yield) gave imidazopyridinyl Ph ketone II. Fourteen compds. I, including II, were tested in a cell growth inhibition assay and found to efficiently inhibit growth of KB cells and MKN-45 cells. Most of them exhibited IC<sub>50</sub> values lower than 1 mM, some even lower than 100 nM. Therefore, I and their pharmaceutical compns. are useful for treating diseases such as cancer.

#### MSTR 1A



G1 = alkoxy <containing 1-10 C> (opt. substd.)  
 G2 = 117-135 118-137 120-3



G4 = 47 / N

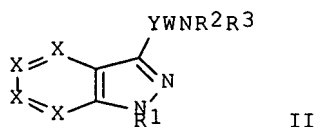
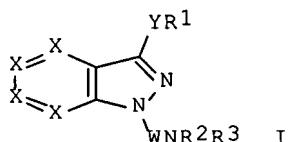
49—G12

Patent location: claim 1  
 Note: substitution is restricted  
 Note: additional substitution also claimed

L37 ANSWER 21 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 143:211907 MARPAT Full-text  
 TITLE: Preparation of indazoles as inhibitors of hormone-sensitive lipase (HSL).  
 INVENTOR(S): Zoller, Gerhard; Petry, Stefan; Mueller, Guenter; Heuer, Hubert; Baringhaus, Karl-Heinz  
 PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany  
 SOURCE: PCT Int. Appl., 57 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

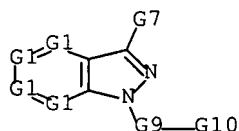
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005073199	A1	20050811	WO 2005-EP365	20050115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004005172	A1	20050818	DE 2004-10200400517220040202	
AU 2005209366	A1	20050811	AU 2005-209366	20050115
CA 2554524	A1	20050811	CA 2005-2554524	20050115
EP 1713779	A1	20061025	EP 2005-700954	20050115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1914180	A	20070214	CN 2005-80003798	20050115
BR 2005007370	A	20070710	BR 2005-7370	20050115
JP 2007519649	T	20070719	JP 2006-549989	20050115
US 2005197348	A1	20050908	US 2005-42565	20050125
IN 2006CN02819	A	20070608	IN 2006-CN2819	20060801
NO 2006003925	A	20060901	NO 2006-3925	20060901
PRIORITY APPLN. INFO.:			DE 2004-10200400517220040202	
			US 2004-582669P	20040624
			WO 2005-EP365	20050115
OTHER SOURCE(S):			CASREACT 143:211907	
GI				

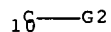


AB Title compds. [I, II; W = CO, SO, SO<sub>2</sub>; X = CR, N; Y = O, NR<sub>1</sub>; R = H, halo, alkyl, OH, alkylthio, amino, CF<sub>3</sub>, alkylaminocarbonyl, NO<sub>2</sub>, F<sub>5</sub>S, etc.; R<sub>1</sub> = H, alkyl, PhCH<sub>2</sub>; R<sub>2</sub> = H, alkyl, (substituted) alkylphenyl, aryl, tetramethyltetrahydronaphthyl; R<sub>3</sub> = H, alkyl; NR<sub>2</sub>R<sub>3</sub> = atoms to form a 4-7 membered monocyclic or 8-14 membered bicyclic (unsatd.) (substituted) ring; with provisos], were prepared Thus, 1H-indazol-3-ol in THF at -20° was treated with COCl<sub>2</sub> in PhMe followed by stirring to room temperature over 90 min. The residue in THF was treated with 4-methylpiperidine followed by stirring for 3 h to give 60% 4-methylpiperidine-1-carboxylic acid 1H-indazol-3-yl ester. Title compds. inhibited HSL with IC<sub>50</sub> = 1 nM-1 μM.

MSTR 1



G1 = 10 / N



G2 = OH

Patent location:

Note:

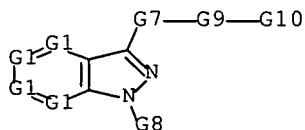
Note:

claim 1

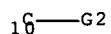
and physiologically acceptable salts and tautomeric forms

substitution is restricted

## MSTR 2



G1 = 10 / N



G2 = OH

Patent location:

Note:

Note:

claim 1

and physiologically acceptable salts and tautomeric forms

substitution is restricted

REFERENCE COUNT:

8

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 22 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 142:261532 MARPAT Full-text

TITLE: Preparation of benzoindazole compounds as gabanergic modulators

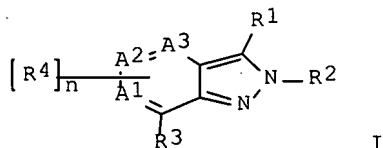
INVENTOR(S): Lin, Xiao-fa; Loughhead, David Garrett; Novakovic, Sanja; O'Yang, Counde; Putman, David George; Soth, Michael



PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 130 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016892	A1	20050224	WO 2004-EP8767	20040805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004265101	A1	20050224	AU 2004-265101	20040805
CA 2535406	A1	20050224	CA 2004-2535406	20040805
EP 1656353	A1	20060517	EP 2004-763813	20040805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004013540	A	20061010	BR 2004-13540	20040805
CN 1852897	A	20061025	CN 2004-80026535	20040805
JP 2007502257	T	20070208	JP 2006-522959	20040805
US 2005101614	A1	20050512	US 2004-916073	20040811
MX 2006PA01660	A	20060428	MX 2006-PA1660	20060210
IN 2006CN00533	A	20070622	IN 2006-CN533	20060213
PRIORITY APPLN. INFO.:				
			US 2003-495179P	20030814
			US 2004-574384P	20040525
			WO 2004-EP8767	20040805

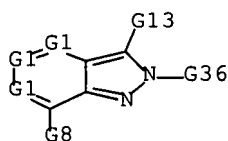
OTHER SOURCE(S): CASREACT 142:261532  
 GI



AB Title compds. I [R1 = alkynyl, haloalkyl, halo, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3 = (un)substituted aryl, (un)substituted heteroaryl with alkyl, alkoxy, alkylthio, etc.; R4 = alkyl, alkoxy, haloalkyl, etc.; n = 0-p, where p = 3 minus the number of A1, A2 and A3 which are nitrogen; A1, A2, A3 = C, N with the proviso that at least one of A1, A2 and A3 is CH or CR4] and their pharmaceutically acceptable salts were prepared For example, bromination of 7-(2,4-dichlorophenyl)-2-methyl-2H-indazole afforded 3-bromo-7-(2,4-dichlorophenyl)-2-methyl-2H-indazole (II) in 62% yield. The exemplified

compound II was tested in GABAA  $\alpha 1\beta 2\gamma 2$  binding assay, exhibited the pIC50 value of 6.24. Comps. I are claimed useful for the treatment of depression, convulsive disorder, etc. Formulations are given.

# MSTR 1



G1 = 11 / N

1f—G2

G2 = alkoxy <containing 1-10 C>

Patent location: claim 1

Note: or solvates, hydrates or pharmaceutically acceptable salts

Note: also incorporates claim 6

Stereochemistry: individual isomers, racemic or non-racemic mixtures of isomers

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 23 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 142:155976 MARPAT Full-text

TITLE: Preparation of imidazo[1,2-a]pyrazin-8-ylamines as Bruton's tyrosine kinase (Btk) inhibitors for the treatment of cancer

INVENTOR(S): Currie, Kevin S.; Desimone, Robert W.; Mitchell, Scott; Pippin, Douglas A.

PATENT ASSIGNEE(S): Cellular Genomics, Inc., USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005429	A1	20050120	WO 2004-US21150	20040630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

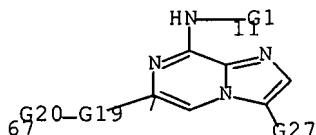
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

US 2005101604 A1 20050512 US 2004-883646 20040630  
 PRIORITY APPLN. INFO.: US 2003-484014P 20030630  
 OTHER SOURCE(S): CASREACT 142:155976  
 GI

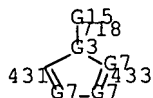
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [X = -Z2-Q-R2; Z2 = divalent linking group, i.e., para-phenylene, meta-phenylene, ortho-phenylene, etc.; Q = CON(R4), N(R4)CO; R1 = (un)substituted indole, indazole, benzoxazole, etc.; R2 = alkyl, cycloalkyl, heterocycloalkyl, etc.; R3 = H, alkyl, heterocycloalkyl, etc.; R4 = H, alkyl, (un)substituted Ph etc.] and their pharmaceutically acceptable salts were prepared For example, p-tert-Bu benzoyl chloride acylation of aniline II, i.e., prepared from 3,5-dibromo-2-aminopyrazine in 3-steps, afforded claimed imidazopyrazinylamine III. Compds. I are claimed to be useful for the treatment of cancer, autoimmune and/or inflammatory disease or acute inflammatory reaction.

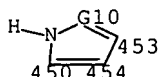
# MSTR 1



G1 = 431



G3 = 450-431 454-433 453-718



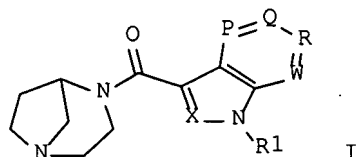
G7 = (up to 1) N / 567

G10 = N  
 G12 = OMe  
 Patent location: claim 1  
 Note: or pharmaceutically acceptable salts  
 Note: additional oxo formation and substitution also  
 claimed

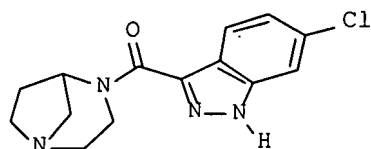
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 24 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 143:133407 MARPAT Full-text  
 TITLE: Preparation of 1,4-diazabicyclo[3.2.1]octanecarboxamid  
 es as ligands for nicotinic receptors, especially  
 $\alpha 4\beta 2$  and  $\alpha 7$  subunits, for treating  
 central nervous system diseases  
 INVENTOR(S): Galli, Frederic; Leclerc, Odile; Lochead, Alistoir W.  
 PATENT ASSIGNEE(S): Sanofi-Synthelabo S.A., Fr.  
 SOURCE: Fr. Demande, 22 pp.  
 CODEN: FRXXBL  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2865208	A1	20050722	FR 2004-390	20040116
AU 2005212867	A1	20050825	AU 2005-212867	20050107
CA 2549954	A1	20050825	CA 2005-2549954	20050107
WO 2005077955	A1	20050825	WO 2005-FR27	20050107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1709052	A1	20061011	EP 2005-717375	20050107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1946726	A	20070411	CN 2005-80002630	20050107
BR 2005006879	A	20070612	BR 2005-6879	20050107
JP 2007517838	T	20070705	JP 2006-548338	20050107
IN 2006KN01850	A	20070511	IN 2006-KN1850	20060703
US 2007155749	A1	20070705	US 2006-456345	20060710
MX 2006PA07984	A	20061019	MX 2006-PA7984	20060712
NO 2006003666	A	20061011	NO 2006-3666	20060814
PRIORITY APPLN. INFO.:			FR 2004-390	20040116



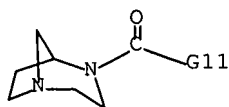
I



II

AB Title compds. I [wherein X = N, CR<sub>2</sub>, P = CR<sub>3</sub>, Q = CR<sub>4</sub>; R = CR<sub>5</sub>; W = CR<sub>6</sub>, or one of P, Q, R, W = N; R<sub>1</sub>, R<sub>2</sub> = independently H, alkyl; R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> = independently H, halo, alkyl, alkoxy, NO<sub>2</sub>, NH<sub>2</sub> and derivs., CF<sub>3</sub>, CN, NHCO<sub>2</sub>H and derivs., OH and derivs., SH and derivs., CO<sub>2</sub>H and derivs., CONH<sub>2</sub> and derivs., etc.; R<sub>3</sub>CCR<sub>4</sub>, R<sub>4</sub>CCR<sub>5</sub>, R<sub>5</sub>CCR<sub>6</sub> = (un)substituted hetero/aromatic 6-membered; their free bases and salts of addition with acids] were prepared as CNS agents, and specifically as ligands of nicotinic receptor. The compds. were tested against nicotinic receptors with the  $\alpha 4\beta 2$  subunit or with the  $\alpha 7$  subunit. Thus, reacting 3-iodo-6-chloro-1H-indazole with 1,4-diazabicyclo[3.2.1]octane and CO in the presence of TEA/DMF at 70° for 8 h gave II•HCl (m.p. = 285-286°). In tests for specific binding to isolated rat cerebral nicotinic receptors having either  $\alpha 4\beta 2$  or  $\alpha 7$  subunits, compds. I displayed IC<sub>50</sub> values in the ranges of 1-10  $\mu$ M and 0.01-0.1  $\mu$ M, resp. I showed selectivity for the  $\alpha 7$  receptor subtype.

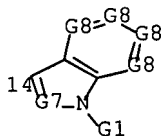
#### MSTR 1



G3 = alkoxy <containing 1-6 C>  
 G7 = N  
 G8 = N / 177

197—G3

G11 = 14



Patent location: claim 1  
Note: or acid addition salts or solvates  
Stereochemistry: and enantiomers

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 25 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 142:38528 MARPAT Full-text

TITLE: Preparation of 1,1-disubstituted cycloalkyl-,  
glycinamidyl-, sulfonylamidino-, and  
tetrahydropyrimidinyl-containing diaminoalkanes and  
 $\beta$ - or  $\alpha$ -amino acids and their derivatives  
as factor Xa inhibitors

INVENTOR(S): Qiao, Jennifer X.; Pinto, Donald J.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 183 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

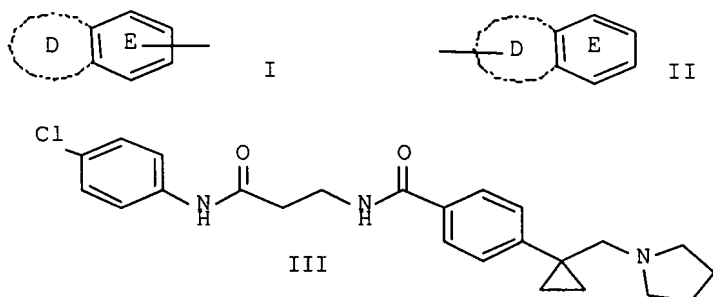
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

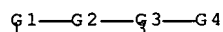
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108892	A2	20041216	WO 2004-US17296	20040602
WO 2004108892	A3	20050217		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004266761	A1	20041230	US 2004-858084	20040601
US 7250415	B2	20070731		
EP 1628668	A2	20060301	EP 2004-754003	20040602
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
JP 2006526653	T	20061124	JP 2006-515071	20040602
PRIORITY APPLN. INFO.:			US 2003-475731P	20030604
			WO 2004-US17296	20040602

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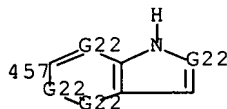


AB The invention relates to compds. P-M-M1 [one of P and M1 = G and the other - AB; G = I or II, where ring D, including the two carbon atoms of ring E to which it is attached, is (un)substituted 5-6 membered ring consisting of carbon atoms and 0-3 heteroatoms selected from N, O, S(O)0-2; ring D may contain 0-3 ring double bonds; ring E = (un)substituted Ph, pyridyl, pyrimidyl, etc.; alternatively, ring D is absent; A = (un)substituted C3-10 carbocyclyl or 5-12 membered heterocyclyl; B = X-Y-R4a, -N(B1)COC(R3R3g)1-4NB2B3, C(B4):NB4 or a related 5-8 membered ring, where X is (un)substituted alkylene, CO, SO2, etc.; Y is carbocyclyl or heterocyclyl; B1-B3 are H, (un)substituted alkyl, etc.; R4 is sulfonyl or acyl groups, CN, etc.; R5 is (un)substituted amino or alkyl; R3, R3g, R4a are H, alkyl, etc.; M = (un)substituted 3-8 membered linear chain consisting of carbon atoms, (thio)carbonyl groups, and/or heteroatoms with 0-2 double bonds and 0-1 triple bond] or their stereoisomers, pharmaceutically-acceptable salts, solvates or prodrugs, which are useful as inhibitors of trypsin-like serine proteases, specifically factor Xa, for treating thromboembolic disorder. Thus, compound III was prepared by a multistep procedure which includes coupling of 1-(4-chlorocarbonylphenyl)cyclopropanecarboxylic acid Me ester with  $\beta$ -alanine tert-Bu.

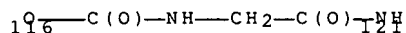
#### MSTR 1



G1 = 457



G2 = 116-1 121-3



G22 = N / CH

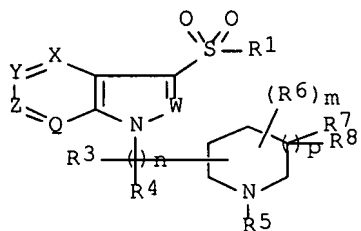
Patent location: claim 1  
 Note: or pharmaceutically acceptable salts or solvates  
 Note: substitution is restricted  
 Note: additional substitution also claimed

L37 ANSWER 26 OF 40 MARPAT' COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 140:146118 MARPAT Full-text  
 TITLE: Preparation of heterocyclylalkyl-sulfonylazaindole or  
 -azaindazole derivatives 5-hydroxytryptamine-6 (5-HT6)  
 ligands  
 INVENTOR(S): Bernotas, Ronald Charles; Lenicek, Steven Edward;  
 Elokdah, Hassan Mahmoud; Li, David Zenan  
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA  
 SOURCE: PCT Int. Appl., 50 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

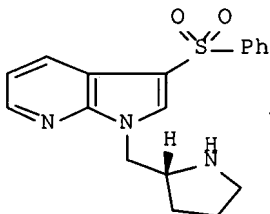
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009600	A1	20040129	WO 2003-US22506	20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491251	A1	20040129	CA 2003-2491251	20030717
US 2004023970	A1	20040205	US 2003-621432	20030717
US 7057039	B2	20060606		
AU 2003254002	A1	20040209	AU 2003-254002	20030717
BR 2003012758	A	20050426	BR 2003-12758	20030717
EP 1551840	A1	20050713	EP 2003-765726	20030717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1668620	A	20050914	CN 2003-816980	20030717
JP 2005536521	T	20051202	JP 2004-523566	20030717
NO 2005000007	A	20050411	NO 2005-7	20050103
MX 2005PA00650	A	20050331	MX 2005-PA650	20050114
IN 2005KN00158	A	20060609	IN 2005-KN158	20050209
US 2006142330	A1	20060629	US 2006-354459	20060215
PRIORITY APPLN. INFO.:			US 2002-396949P	20020718
			US 2003-621432	20030717
			WO 2003-US22506	20030717

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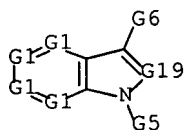
I



II

AB Title compds. I [W, X, Y, Z, Q = N, substituted C; R1 = (cyclo)alkyl, (hetero)aryl, etc.; R2 = H, halo, alkyl, alkoxy, etc.; R3-4 = H, alkyl; R5 = H, alk(en/yn)yl, etc.; R6 = alk(en/yn)yl, cycloalkyl, etc.; R7-8 = H, alk(en/yn)yl, cycloalkyl, etc.; m, n = 0-3; p = 0-2] are prepared For instance, 3-(Phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (preparation given) is reacted with tert-Bu (2R)-2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-1-pyrrolidinecarboxylate (i. DMF, NaH, 0°; ii. dioxane, HCl, 4 h) to give II•HCl. II has Ki = 12 nM for the 5-HT6 receptor. I are useful for treatment of a central nervous system disorder related to or affected by the 5-HT6 receptor.

#### MSTR 1



G1 = (1-2) N / 372

392—G2

G2 = 23

29—C(O)-G3

G19 = N

Patent location:

Note:

Note:

Stereochemistry:

claim 1

or pharmaceutically acceptable salts

also incorporates claims 20 and 21

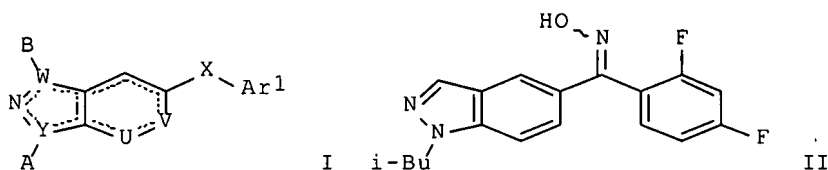
or stereoisomers

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 27 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 141:314320 MARPAT Full-text  
 TITLE: Preparation of indazoles and related compounds as p38 inhibitors  
 INVENTOR(S): Munson, Mark; Mareska, David A.; Kim, Youngboo; Groneberg, Robert D.; Rizzi, James; Rodriguez, Martha; Kim, Ganghyeok; Vigers, Guy; Rao, Chang; Balachari, Devan; Harvey, Darren  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 139 pp., Cont.-in-part of U.S. Ser. No. 688,849.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192653	A1	20040930	US 2004-788044	20040225
US 2004176325	A1	20040909	US 2003-378164	20030303
US 7135575	B2	20061114		
US 2004180896	A1	20040916	US 2003-688849	20031015
PRIORITY APPLN. INFO.:			US 2003-378164	20030303
			US 2003-688849	20031015

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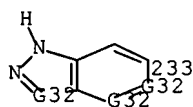
AB The invention provides for the preparation of the title compds. I [Y = C, N; W = C, N, S, provided that W = N, S, or O when Y = C, and W = C or N when Y = N; U = CH, N; V = C(E), N; X = O, S, SO, SO<sub>2</sub>, etc.; Ar1 = (un)substituted (hetero)aryl; A = H, OH, an amine protecting group, etc.; B = H, NH<sub>2</sub>, (un)substituted Me; E = H, OH, an amine protecting group, etc.; with the provisos; and stereoisomers, solvates, and pharmaceutically acceptable salts thereof] as p38 MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH<sub>4</sub>BF<sub>4</sub> provided 5-bromo-1H-indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with NH<sub>2</sub>OH•HCl (65.5%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The latter inhibited p38α activity and LPS-induced TNF-α secretion from human peripheral blood mononuclear cells (PBMC) with IC<sub>50</sub> values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by p38, such as

inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

**MSTR 1**

G45—G2—G1

G2 = O  
G32 = N / CH  
G45 = 233



Patent location: claim 1  
Note: additional substitution and heteroatom interruptions also claimed  
Note: and solvates and pharmaceutically acceptable salts  
Note: also incorporates claim 27  
Stereochemistry: and resolved enantiomers, diastereomers

L37 ANSWER 28 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 141:260746 MARPAT Full-text  
TITLE: Preparation of indazoles and related compounds as p38 inhibitors  
INVENTOR(S): Munson, Mark; Kim, Youngboo; Groneberg, Robert D.; Rizzi, James; Rodriguez, Martha; Kim, Ganghyeok; Vigers, Guy; Rao, Chang; Balachari, Devan  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 118 pp., Cont.-in-part of U.S. Pat. Appl. 2004 176,325.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2004180896	A1	20040916	US 2003-688849	20031015
US 2004176325	A1	20040909	US 2003-378164	20030303
US 7135575	B2	20061114		
AU 2004218463	A1	20040916	AU 2004-218463	20040225
CA 2517517	A1	20040916	CA 2004-2517517	20040225
WO 2004078116	A2	20040916	WO 2004-US5693	20040225
WO 2004078116	A3	20041014		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

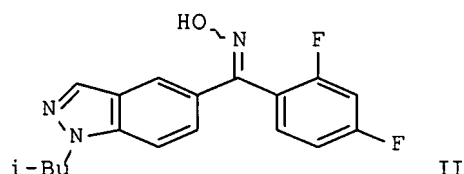
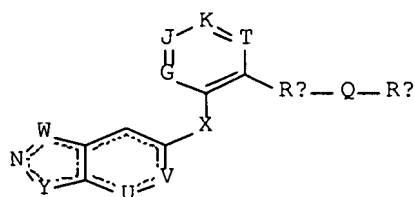
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 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004192653 A1 20040930 US 2004-788044 20040225  
 EP 1606283 A2 20051221 EP 2004-714621 20040225  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 CN 1784396 A 20060607 CN 2004-80011990 20040225  
 JP 2006519259 T 20060824 JP 2006-508838 20040225  
 MX 2005PA09459 A 20060517 MX 2005-PA9459 20050902  
 NO 2005004453 A 20051129 NO 2005-4453 20050926

PRIORITY APPLN. INFO.:

US 2003-378164 20030303  
 US 2003-688849 20031015  
 WO 2004-US5693 20040225

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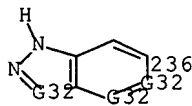
AB The invention provides for the preparation of title compds. I [wherein G, J, K, T = independently NCRz; Q = NR8CONH, NHCO, NR8SO2NH, NHSO2, COR11; U, V = (un)substituted CH, N; W = CR3, N, NR4; X = O, S, SO, SO2, NR5, CO, CH2, CH2ZnOH, C=NORd; Y = CR1, O, S, NR2; Z = (un)substituted alk(en/yn)ylene; R1, R2 = independently H, OH, amine-protecting group, ZnNRaRb, ZnNRaCORb, ZnSO2Ra, ZnSORa, ZnSRa, ZnORa, ZnCORa, ZnCO2Ra, ZnOCORa, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; R3 = H, NH2, F, Cl, (un)substituted Me; R4, R5 = independently H, (un)substituted Me; R6 = H, CF3, (hetero)alkyl; R8, R11 = independently H, alkyl; Ra, Rb = independently H, OH, amine-, alc.-, or sulfur-protecting group, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; or NRaRb = (un)substituted heterocyclyl; Rd = H, PO3H2, SO3H, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; Rx = (un)substituted (CH2)m, O(CH2)m, NH(CH2)m, S(CH2)m; Ry = H, PO3H2, amine- or oxygen-protecting group, (un)substituted (hetero)alk(en/yn)yl, (hetero)alkoxy, Zn-(hetero)cycloalkyl, ZnAr1; Rz = H, F, Cl, Br, CF3, OR6, SR6, alkyl, CN, (un)substituted NH2; Ar1 = (un)substituted (hetero)aryl; m = 1-3; with provisos; and stereoisomers, solvates, and pharmaceutically acceptable salts thereof] as p38 MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH4BF4 provided 5-bromo-1H-

indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with  $\text{NH}_2\text{OH}\cdot\text{HCl}$  (43.1%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The latter inhibited p38 $\alpha$  activity and LPS-induced TNF- $\alpha$  secretion from human peripheral blood mononuclear cells (PBMC) with  $\text{IC}_{50}$  values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by p38, such as inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

#### MSTR 1

G45—G2—G1

G2 = O  
G32 = N / CH  
G45 = 236



Patent location: claim 1  
Note: additional substitution and heteroatom interruptions also claimed  
Note: and solvates and pharmaceutically acceptable salts  
Note: also incorporates broader disclosure  
Stereochemistry: and resolved enantiomers, diastereomers

L37 ANSWER 29 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 141:260742 MARPAT Full-text  
TITLE: Preparation of indazoles and related compounds as p38 inhibitors  
INVENTOR(S): Munson, Mark; Rizzi, James; Rodriguez, Martha; Kim, Ganghyeok  
PATENT ASSIGNEE(S): Array Biopharma, Inc., USA  
SOURCE: U.S. Pat. Appl. Publ., 87 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 2004176325	A1	20040909	US 2003-378164	20030303
US 7135575	B2	20061114		

US 2004180896	A1	20040916	US 2003-688849	20031015
AU 2004218463	A1	20040916	AU 2004-218463	20040225
CA 2517517	A1	20040916	CA 2004-2517517	20040225
WO 2004078116	A2	20040916	WO 2004-US5693	20040225
WO 2004078116	A3	20041014		

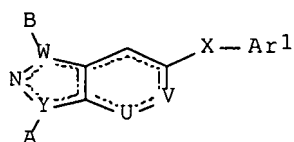
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004192653	A1	20040930	US 2004-788044	20040225
EP 1606283	A2	20051221	EP 2004-714621	20040225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007993	A	20060307	BR 2004-7993	20040225
CN 1784396	A	20060607	CN 2004-80011990	20040225
JP 2006519259	T	20060824	JP 2006-508838	20040225
MX 2005PA09459	A	20060517	MX 2005-PA9459	20050902
NO 2005004453	A	20051129	NO 2005-4453	20050926

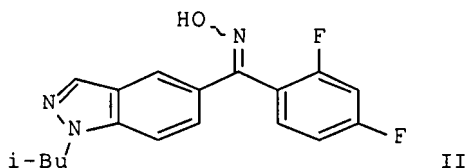
PRIORITY APPLN. INFO.:

US 2003-378164	20030303
US 2003-688849	20031015
WO 2004-US5693	20040225

GI



I



II

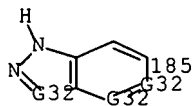
AB The invention provides for the preparation of title compds. I [wherein Y = C, N; W = C, N, S, O; U = CH, N; V = (un)substituted CH, N; X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>, CO, CHR<sub>7</sub>, C=NOR<sub>1</sub>, C=CHR<sub>1</sub>, CHOR<sub>1</sub>; R<sub>1</sub> = H, PO<sub>3</sub>H<sub>2</sub>, SO<sub>3</sub>H, (un)substituted (hetero)alkyl, (hetero)alkenyl, (hetero)alkynyl, (hetero)alkoxy, (hetero)cycloalkylalkyl, (hetero)arylalkyl, etc.; R<sub>7</sub> = H, (un)substituted Me; Ar<sub>1</sub> = (un)substituted (hetero)aryl; A = H, OH, amine protecting group, (un)substituted (hetero)alkyl, (hetero)alkenyl, (hetero)alkynyl, (hetero)alkoxy, (hetero)cycloalkylalkyl, (hetero)arylalkyl, etc.; B = H, NH<sub>2</sub>, (un)substituted Me; with provisos; and enantiomers diastereomers, solvates, and pharmaceutically acceptable salts thereof] as p38 MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH<sub>4</sub>BF<sub>4</sub> provided 5-bromo-1H-indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with NH<sub>2</sub>OH•HCl (43.1%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The latter inhibited p38α activity and LPS-induced TNF-α secretion from human peripheral blood mononuclear cells (PBMC) with IC<sub>50</sub> values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the

inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by p38, such as inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

**MSTR 1**

G34—G2—G1

G2 = O  
G32 = N / CH  
G34 = 185



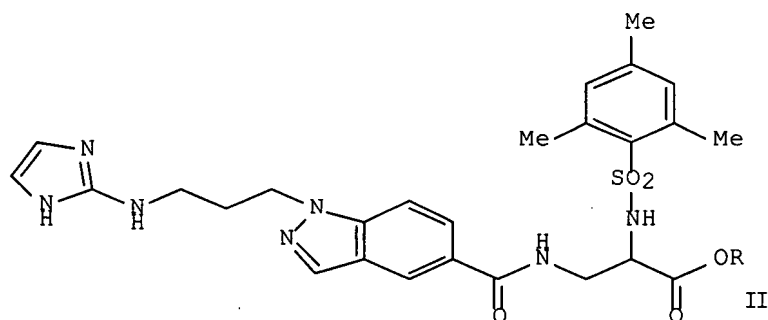
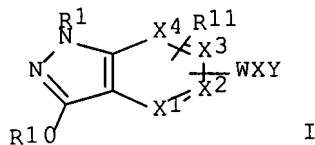
Patent location: claim 1  
Note: additional substitution and heteroatom interruptions also claimed  
Note: and solvates and pharmaceutically acceptable salts  
Stereochemistry: and resolved enantiomers, diastereomers

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 30 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 129:302639 MARPAT Full-text  
TITLE: Preparation of imidazolylaminopropylindazolylcarbonylaminopropionate ammonioalkyl esters and related compounds as integrin  $\alpha v \beta 3$  inhibitor prodrugs.  
INVENTOR(S): Jadhav, Prabhakar; Batt, Douglas G.; Hussain, Munir A.; Pitts, William J.; Repta, Arnold J.  
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Co., USA  
SOURCE: PCT Int. Appl., 311 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843962	A1	19981008	WO 1998-US6054	19980327
W: AU, BR, CA, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9867803	A	19981022	AU 1998-67803	19980327
US 6214834	B1	20010410	US 1998-49305	19980327

GI



AB Title compds. [I; X1-X4 = N, C;  $\geq 2$  of X1-X4 = C; R1 = specified heterocyclalkyl; R10 = H, amino, halo, NO<sub>2</sub>, cyano, CF<sub>3</sub>, sulfonylamino, carbamoyl, (substituted) alkyl, alkoxy, alkenyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, etc.; R11 = H, halo, CF<sub>3</sub>, cyano, NO<sub>2</sub>, OH, amino, (substituted) alkyl, alkoxy, aryl, aralkyl, alkoxycarbonyl, alkylcarbonyl, alkylsulfonyl, alkylaminosulfonyl; W = [C(R12)<sub>2</sub>]qCONR13, CONR13[C(R12)<sub>2</sub>]q; X = CR12R14CR12R15; WX = specified piperazinylcarbonyl(alkyl); Y = COR19; R12 = H, halo, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, alkylcarbonyl, aryl, aralkyl; R13 = H, (substituted) alkyl, cycloalkylmethyl, aralkyl; R14 = H, alkylthioalkyl, aralkylthioalkyl, aralkoxyalkyl, alkyl, alkoxyalkyl, hydroxyalkyl, alkenyl, alkynyl, cycloalkyl, aralkyl, heteroarylalkyl, aryl, heteroaryl, etc.; R15 = H, (substituted) alkyl, alkoxyalkyl, alkylaminoalkyl, aralkylcarbonyl, aryl, heteroaryl, heteroarylalkyl, aminosulfonyl, aminosulfonylamino, etc.; R19 = O(CH<sub>2</sub>)<sub>k</sub>N+R22R23R24 Z<sup>-</sup>; Z<sup>-</sup> = specified pharmaceutically acceptable anion; R22-R24 = H, (substituted) alkyl, cyclolalkylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl; R22R23 = (substituted) 5-7 membered heterocyclyl; R22R23R24 = (substituted) heterobicyclyl; q = 0-2; k = 2-6], were prepared I may be administered by iontophoresis for the inhibition of cell adhesion, the treatment of angiogenic disorders, inflammation, bone degradation, cancer metastasis, diabetic retinopathy, thrombosis, restenosis, macular degeneration, and other conditions mediated by cell adhesion and/or cell migration and/or angiogenesis. Thus, title compound (II; R = CH<sub>2</sub>CH<sub>2</sub>N+Me<sub>3</sub>) showed electrophoretic mobility = 3.2 cm<sup>2</sup>/V/s at pH 4.5, vs. 1.7 cm<sup>2</sup>/V/s for II (R = Me).

MSTR 1A



~~128~~~~9~~—~~G4~~—~~G1~~—~~G19~~—~~309~~—~~G17~~—~~G20~~

G1 = 62

~~62~~<sup>30</sup>—~~63~~<sup>31</sup>

G2 = N / 13

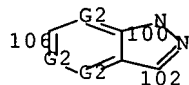
~~13~~—G3

G4 = 130-129 131-2 / 132-129 133-2 / 134-129 136-2

~~130~~—~~131~~    ~~132~~—~~133~~    ~~134~~—G5—~~136~~

G5 = O

G30 = 106-1 100-63 102-3



Derivative:	or pharmaceutically acceptable salts
Patent location:	claim 1
Note:	additional ring formation also claimed
Note:	substitution is restricted
Note:	also incorporates claims 6 and 11
Stereochemistry:	including stereoisomeric forms or mixtures of stereoisomeric forms

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 31 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 128:128015 MARPAT Full-text

TITLE: Preparation of amidinoindoles and amidinoazoles as inhibitors of factor Xa and of thrombin

INVENTOR(S): Dominguez, Celia; Han, Qi; Duffy, Daniel Emmett; Park, Jeongsook Maria; Quan, Mimi Lifan; Rossi, Karen Anita; Wexler, Ruth Richmond

PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Co., USA

SOURCE: PCT Int. Appl., 176 pp.

CODEN: PIXXD2

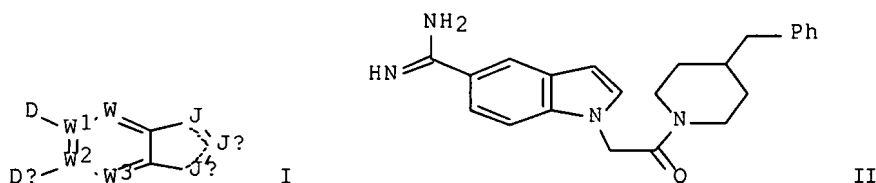
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

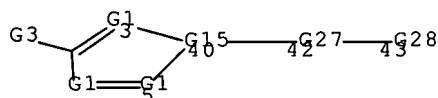
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9801428	A1	19980115	WO 1997-US11325	19970630
W: AM, AU, AZ, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2259573	A1	19980115	CA 1997-2259573	19970630
AU 9736456	A	19980202	AU 1997-36456	19970630
EP 960102	A1	19991201	EP 1997-933214	19970630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
NZ 333696	A	20000623	NZ 1997-333696	19970630
PRIORITY APPLN. INFO.:				
			US 1996-676766	19960708
			US 1997-49519P	19970613
			WO 1997-US11325	19970630

GI



AB The title compds. [I; W, W3 = CH, N; W1, W2 = C, CH, N (provided that one of W1 and W2 is C(C(=NH)NH2) and at most two of W, W1, W2, and W3 are N); one of D, Da = H, C1-4 alkoxy, CN, etc. and the other is absent; one of Ja and Jb is substituted by -(CH2)n-Z-A-B; J, Ja, Jb combine to form an aromatic heterocyclic system containing from 1-2 heteroatoms (N, O, and S), a heterocyclic ring wherein Jb = N and J and Ja = (un)substituted CH2, a heterocyclic ring wherein Jb = CH, J = (un)substituted NH and Ja = (un)substituted CH; Z = CH:CH, SO2CH2, etc.; A = (un)substituted PhCH2, PhCH2CH2, etc.; B = C3-6 alkyl, (un)substituted PhCH2, 5-10 membered heterocyclic system, etc.], useful as inhibitors of factor Xa or thrombin, were prepared and formulated. Thus, reaction of 5-cyanoindole-1-acetic acid with 4-benzylpiperidine followed by treatment of the resulting 1-(4-benzylpiperidinocarbonyl)methyl-5-cyanoindole with HCl(g) in MeOH, and then with (NH4)2CO3 in MeOH afforded the title compound II. Some compds. I were evaluated and showed Ki of < 5 μM against thrombin.

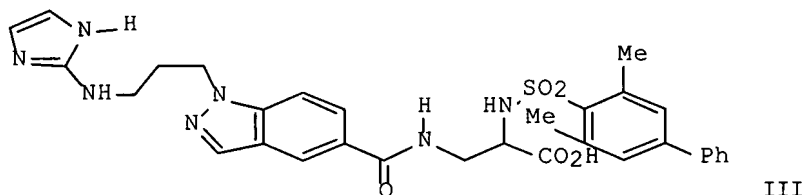
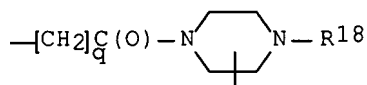
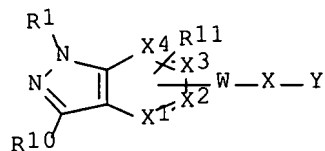
#### MSTR 1A



C1=CN(C=C1)N

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5760028	A	19980602	US 1996-770538	19961220
PRIORITY APPLN. INFO.:			US 1996-770538	19961220



AB The title compds. [I; X1-X4 = N, C (at least two of X1-X4 = C); R1 = 2-aminopyridin-6-yl(CH2)2, pyridin-2-ylamino(CH2)3, imidazol-2-ylamino(CH2)3, etc.; R10 = H, halo, NO2, etc.; R11 = H, halo, CF3, etc.; W = [C(R12)2]qC(O)NR13 (wherein R12 = H, halo, C1-6 alkyl, etc.; R13 = H, C1-6 alkyl, C3-7 cycloalkylmethyl, etc.; q = 0-2), C(O)NR13[C(R12)2]q; X = C(R12)(R14)C(R12)(R15) (R14 = H, C1-10 alkyl, C2-10 alkenyl, etc.; R15 = H, C1-10 alkyl, C1-10 alkoxyalkyl, etc.); WX = II (R18 = H, C(O)OR17, C(O)R17, etc.; R17 = C1-10 alkyl, C3-11 cycloalkyl, etc.); Y = SO3H, PO3H, tetrazolyl, etc.] including 3-{1-[3-(imidazolin-2-ylamino)propyl]indazol-5-ylcarbonylamino}-2-(benzyloxycarbonylamino)propionic acid, useful as antagonists of the  $\alpha\beta$ 3 integrin and related cell surface adhesive protein receptors, for the inhibition of cell adhesion, the treatment of angiogenic disorders, inflammation, bone degradation, cancer metastasis, diabetic retinopathy, thrombosis, restenosis, macular degeneration, and other conditions mediated by cell adhesion and/or cell migration and/or angiogenesis, were prepared. Thus, e.g., multi-step synthesis of the title compound 2(S)-III.CF3COOH is described. Compds. I are effective at 0.001-10 mg/kg/day.

# MSTR 1A

128-14-21-317

G1 = 62

6230-631

G2 = N / 13

13-G3

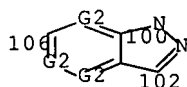
G4 = 130-129 131-2 / 132-129 133-2 / 134-129 136-2

135-136 132-133 134-G5-136

G5 = O

G25 = bond

G30 = 106-1 100-63 102-3



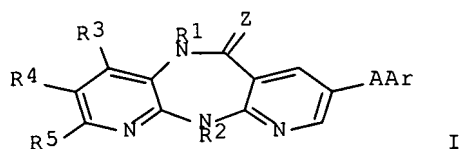
Derivative: and pharmaceutically acceptable salts  
 Patent location: claim 1  
 Note: additional ring formation also claimed  
 Note: substitution is restricted  
 Note: also incorporates claims 6 and 11

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

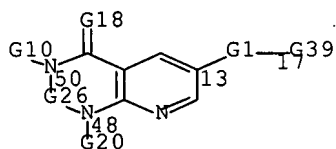
L37 ANSWER 33 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 128:114968 MARPAT Full-text  
 TITLE: Preparation of 8-aralkyl-5,11-dihydro-6H-dipyrido[3,2-b:2',3'-e][1]diazepines for treatment of HIV-1 infection.  
 INVENTOR(S): Cywin, Charles L.; Hoermann, Maryann; Klunder, Janice M.  
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA  
 SOURCE: U.S., 39 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5705499	A	19980106	US 1996-710996	19960925
PRIORITY APPLN. INFO.:			US 1996-710996	19960925

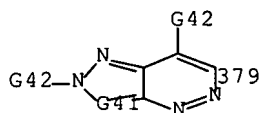
GI



AB Title compds. [I; A = chain of 1-3 atoms, cyclopropylene, oxiranylene; Ar = (substituted) 5-6 membered (hetero)aryl; R1 = H, alkyl, fluoroalkyl, alkenylmethyl, alkynylmethyl, (substituted) aryl, arylmethylalkanoyl, thioalkanoyl, alkylsulfonyl, etc.; Z = O, S, NCN, alkoximino; R2 = H, alkyl, fluoroalkyl, cycloalkyl, oxetanyl, thietanyl, tetrahydrofuryl, alkenylmethyl, alkynylmethyl, alkoxyalkyl, alkylthioalkyl, alkanoyl, cyano, cyanoalkyl, hydroxyalkyl, acyloxyalkyl, etc.; R3 = H, alkyl, alkenyl, alkynyl, trihalomethyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, halo; R4 = H, Me, halo; R5 = H; R3R4 or R4R5 = cycloalkyl; with provisos], were prepared Thus, 2-chloro-5,11-dihydro-11-ethyl-5-methyl- 8-[2-(pyrid-4-yloxy)ethyl]-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one (preparation given) showed an IC50 = 0.03  $\mu$ M in the syncytia assay using HIV-1 in CD4+ T-cells.



G1 = O  
G39 = 379



G41 = CH (opt. substd.)

Derivative: or pharmaceutically acceptable salts  
Patent location: claim 1

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 34 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 127:136075 MARPAT Full-text

TITLE: Annelated pyrazoles as novel integrin receptor antagonists

INVENTOR(S): Jadhav, Prabhakar Kondaji; Petraitis, Joseph James; Batt, Douglas Guy

PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Company, USA; Jadhav, Prabhakar Kondaji; Petraitis, Joseph James; Batt, Douglas Guy

SOURCE: PCT Int. Appl., 419 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723480	A1	19970703	WO 1996-US20523	19961218
W: AM, AU, AZ, BA, BR, BY, CA, CN, CU, CZ, EE, HU, IL, JP, KG, KR, KZ, LC, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2240439	A1	19970703	CA 1996-2240439	19961218
AU 9713456	A	19970717	AU 1997-13456	19961218
EP 939757	A1	19990908	EP 1996-944984	19961218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000501105	T	20000202	JP 1997-523845	19961218
ZA 9610873	A	19980623	ZA 1996-10873	19961223
PRIORITY APPLN. INFO.:			US 1995-9088P	19951222

US 1996-646663 19960508  
 US 1996-25699P 19960909  
 WO 1996-US20523 19961218

AB This invention relates to novel heterocycles including 3-[1-[3-(imidazolin-2-ylamino)propyl]indazol-5-ylcarbonylamino]-2- (benzyloxycarbonylamino)propionic acid (I), which are useful as antagonists of the  $\alpha\beta3$  integrin and related cell surface adhesive protein receptors (no data). Thus, I was prepared from 3-methyl-4-nitrobenzoic acid by conversion to Et 5-indazolecarboxylate and reaction with 2-methylthio-4,5-dihydroimidazole-HI, followed by (S)-H<sub>2</sub>NCH<sub>2</sub>CH(NHCO<sub>2</sub>CH<sub>2</sub>Ph)CO<sub>2</sub>Et.

**MSTR 1A**

~~129~~—~~G4~~—~~G1~~—~~G17~~

G1 = 62

~~62~~<sup>30</sup>—~~G3~~<sup>31</sup>

G2 = N / 13

~~13~~—G3

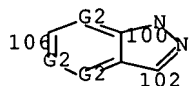
G4 = 130-129 131-2 / 132-129 133-2 / 134-129 136-2

~~130~~—~~131~~    ~~132~~—~~133~~    ~~134~~—G5—~~136~~

G5 = O

G25 = bond

G30 = 106-1 100-63 102-3

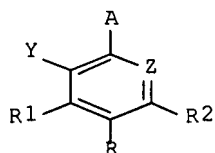


Derivative: ,  
 Patent location:  
 Note:  
 Note:  
 Note:

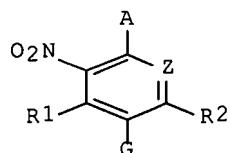
and pharmaceutically acceptable salts  
 claim 1  
 additional ring formation also claimed  
 substitution is restricted  
 also incorporates claims 6 and 11

L37 ANSWER 35 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 127:65763 MARPAT Full-text  
 TITLE: Process for the preparation of pesticidal 1-(haloaryl)  
 heterocyclic compounds  
 INVENTOR(S): Huang, Jamin; Huber, Scot K.; Smith, Philip H. G.;  
 Wilkinson, John H.  
 PATENT ASSIGNEE(S): Rhone-Poulenc Inc., USA  
 SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 426,656,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5631381	A	19970520	US 1996-671691	19960628
AT 189676	T	20000215	AT 1996-105711	19960411
JP 08319272	A	19961203	JP 1996-97106	19960418
BR 9601575	A	19980324	BR 1996-1575	19960419
CN 1182080	A	19980520	CN 1996-106107	19960422
CN 1087735	B	20020717		
US 5726324	A	19980310	US 1997-799455	19970213
CN 1330072	A	20020109	CN 2001-122662	20010627
HK 1042899	A1	20061124	HK 2002-104423	20020613
PRIORITY APPLN. INFO.:			US 1995-426656	19950421
			US 1996-671691	19960628
OTHER SOURCE(S):		CASREACT 127:65763		
GI				



I

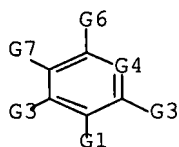


II

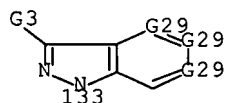
AB The title compds. [I; R = haloalkyl, haloalkoxy, halo, etc.; R1, R2 = H, halo; Y = halo; Z = N, C(NO2), C(CN), etc.; A = (un)substituted N-linked nitrogen-containing 5-6 membered heterocyclic ring], useful as pesticides (no data), were prepared by reacting 1-(nitroaryl)heterocycles II [G = haloalkyl, haloalkoxy, halo, NO2, etc.] with metallic halide salts such as LiCl, in the presence of a nitrite ion scavenging agent such as sulfamic acid, urea, aniline, etc.

MSTR 1





G6 = 133



G29 = (1) G30 / 147

147—G31

G30 = N

G31 = OH

Derivative: or salts

Patent location: claim 1

L37 ANSWER 36 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 126:317394 MARPAT Full-text

TITLE: 8-Arylalkyl- and 8-arylheteroalkyl-5,11-dihydro-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepines and their use in the prevention or treatment of HIV infection

INVENTOR(S): Cywin, Charles L.; Hoermann, Maryann; Klunder, Janice M.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals Inc., USA

SOURCE: Eur. Pat. Appl., 62 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

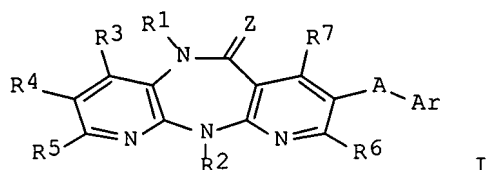
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

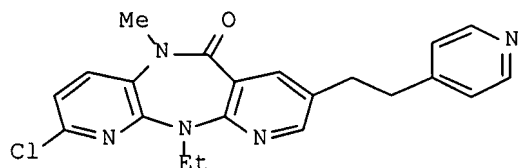
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 767172	A1	19970409	EP 1996-115901	19961004
EP 767172	B1	20030326		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2187146	A1	19970407	CA 1996-2187146	19961004
CA 2187146	C	20060103		
JP 09188680	A	19970722	JP 1996-264860	19961004
AT 235495	T	20030415	AT 1996-115901	19961004
PT 767172	T	20030829	PT 1996-115901	19961004
ES 2191075	T3	20030901	ES 1996-115901	19961004

GI

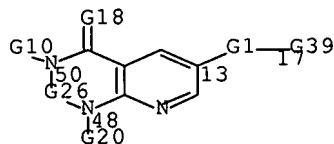


I

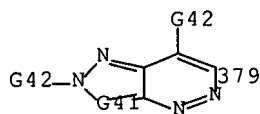


II

AB The invention relates to novel 8-arylalkyl-5,11-dihydro-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepines of general formula I [A = (un)substituted connecting chain of 1-3 atoms, 1,2-cyclopropanediyl, oxiranediyl; Ar = certain (un)substituted (un)fused heteroarom. groups; Z = :O, :S, :NCN, :NOR8; R1 = H, alkyl, fluoroalkyl, alkenylmethyl, (hetero)aryl, alkanoyl, etc.; R2 = H, alkyl, fluoroalkyl, oxetanyl, tetrahydrofuranyl, cyano, oxazolyl, etc.; R3 = alkyl, alkenyl, alkynyl, trihalomethyl, hydroxyalkyl, halo, etc.; R4 = H, Me, halo, and R5 = H; or R3 = R5 = H, and R4 = Me or halo; or R3 = R4 = H, and R5 = alkyl, cycloalkyl, trihalomethyl, hydroxyalkyl, aryloxymethyl, etc.; or R3R4 or R4R5 forms cycloalkyl and R5 or R3 = H; or R3 = R4 = R5 = H; R6 = R7 = H; R8 = alkyl] and their pharmaceutically acceptable salts. The compds. are inhibitors of HIV-1 reverse transcriptase (RT), and are thus useful in the prevention or treatment of HIV infection. For instance, 2-chloro-5,11-dihydro-11-ethyl- 8-iodo-5-methyl-6H-dipyrido[3,2-b:2',3'-e][1,4]diazepin-6-one was coupled with 4-vinylpyridine in the presence of Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> and Et<sub>3</sub>N, and the alkenylated product was reduced by aqueous Na hypophosphite in the presence of Pd black, to give title compound II. In an assay for inhibition of recombinant RT in vitro, II gave 95% inhibition at 1 mM. I were also active in a syncytial assay in human T-cells, and exhibited both high enzymic specificity for HIV-1 RT, and relatively low cytotoxicity in an MTT assay.

**MSTR 1D**

G1 = O  
G39 = 379



G41 = CH (opt. substd.)

Derivative: or pharmaceutically acceptable salts

Patent location: claim 1

L37 ANSWER 37 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 126:104088 MARPAT Full-text

TITLE: Preparation of azahydroxybenzotriazoles and analogs for peptide coupling reactions

INVENTOR(S): Carpino, Louis A.

PATENT ASSIGNEE(S): Research Corporation Technologies, Inc., USA

SOURCE: U.S., 24 pp., Cont.-in-part of U.S. Ser. No. 952,025, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

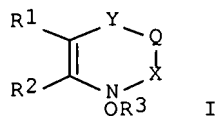
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5580981	A	19961203	US 1993-127675	19930928
US 5644029	A	19970701	US 1995-468300	19950606
US 5698675	A	19971216	US 1995-468593	19950606
US 37686	E1	20020430	US 1998-213298	19981203
US 38073	E1	20030408	US 1999-343756	19990630
PRIORITY APPLN. INFO.:			US 1992-952025	19920928
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			US 1995-468300	19950606

GI

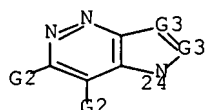


AB Title compds. [I; R1R2 = atoms to complete a heteroarom. ring; R3 = H, alkanoyl, aroyl, etc.; Y = O, NR4, CR4R5; X = CR6R7 or NR6; Q = (CR8R9)n or (NR8)n; R4-R9 = H or alkyl; R4R6 = bond; R6R7 = O; n = 0-2] were prepared as adjuvants for peptide coupling reactions, etc. Thus, 2-nitro-3-methoxypyridine was cyclocondensed with H2NNH2 to give 1-hydroxy-7-azabenzotriazole. Data for examples of reactivity of I were given.

MSTR 2

G1—O—G5

G1 = 24



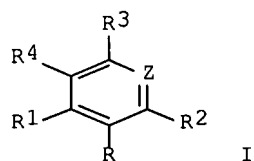
G2 = OH  
G3 = N / 54

G4—G4

Derivative: or N-oxides or salts  
Patent location: claim 30

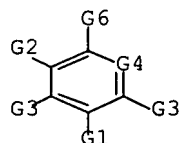
L37 ANSWER 38 OF 40 MARPAT COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 125:328707 MARPAT Full-text  
TITLE: Preparation of N-(haloaryl)heterocyclic compounds  
INVENTOR(S): Huang, Jamin; Huber, Scot Kevin; Smith, Philip Henry  
G.; Wilkinson, John Harry  
PATENT ASSIGNEE(S): Rhone-Poulenc Agrochimie, Fr.  
SOURCE: Eur. Pat. Appl., 16 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 738713	A1	19961023	EP 1996-105711	19960411
EP 738713	B1	20000209		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 189676	T	20000215	AT 1996-105711	19960411
JP 08319272	A	19961203	JP 1996-97106	19960418
BR 9601575	A	19980324	BR 1996-1575	19960419
CN 1182080	A	19980520	CN 1996-106107	19960422
CN 1087735	B	20020717		
CN 1330072	A	20020109	CN 2001-122662	20010627
HK 1042899	A1	20061124	HK 2002-104423	20020613
PRIORITY APPLN. INFO.:			US 1995-426656	19950421
OTHER SOURCE(S):		CASREACT 125:328707		
GI				

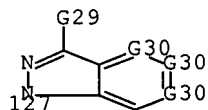


AB The title process comprises treating I (R = halo, haloalkyl, haloalkoxy, etc.; R1, R2 = H or halo; R3 = N-attached heterocyclyl; R4 = NO2; Z = CH, CNO2, CCl, etc.) with a metal halide and a nitrite ion-scavenger to give I (R4 = halo).

**MSTR 1**



G6 = 127



G30 = (2) 234 / N

~~234~~—G39

G39 = OH

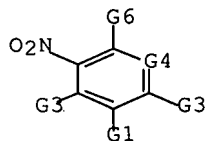
Derivative:

Patent location:

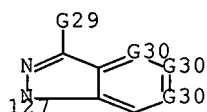
or salts

claim 1

**MSTR 2**



G6 = 127



G30 = (2) 234 / N

~~234~~—G39

G39 = OH

Derivative: or salts

Patent location: claim 1

L37 ANSWER 39 OF 40 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 95:42470 MARPAT Full-text

TITLE: Prostanoid ergolin-8-yl esters, thioesters, and amides

INVENTOR(S): Wenger, Roland

PATENT ASSIGNEE(S): Sandoz A.-G., Switz.

SOURCE: U.S., 9 pp. Cont. of U.S. Ser. No. 773,663, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

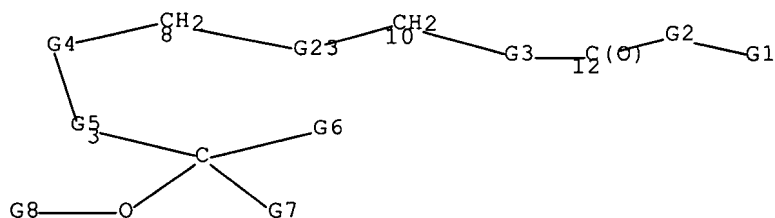
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

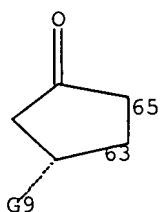
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 4249001	A	19810203	US 1979-55802	19790709
SE 7701916	A	19771028	SE 1977-1916	19770222
AU 7722819	A	19780907	AU 1977-22819	19770301
PRIORITY APPLN. INFO.:			CH 1976-5268	19760427
			CH 1977-2059	19770218
			US 1977-773663	19770302

AB A series of known title compds. was prepared conventionally.

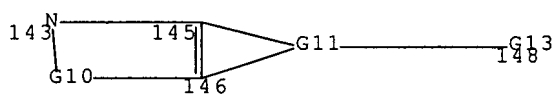
**MSTR 1**



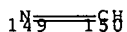
G4 = 63-3 65-8



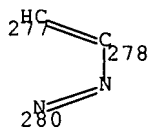
G9 = 143



G10 = 149-143 150-146



G11 = 277-145 278-148 280-146



G13 = alkoxy <containing 1-5 C>

Patent location: claims

Note: record may include structures from disclosure

=> d his full ^

(FILE 'HOME' ENTERED AT 11:18:44 ON 20 AUG 2007)

FILE 'REGISTRY' ENTERED AT 11:19:02 ON 20 AUG 2007

L1 STRUCTURE UPLOADED  
L2 4 SEA SSS SAM L1  
L3 STRUCTURE UPLOADED  
L4 4 SEA SSS SAM L3  
D SCA  
L5 80 SEA SSS FUL L3  
SAVE TEMP L5 WAR219STR3L/A

FILE 'ZCAPLUS' ENTERED AT 11:22:38 ON 20 AUG 2007

L6 17 SEA ABB=ON PLU=ON L5  
L7 3886 SEA ABB=ON PLU=ON GREEN J?/AU  
L8 285 SEA ABB=ON PLU=ON GREY R?/AU  
L9 422 SEA ABB=ON PLU=ON PIERCE A?/AU  
L10 2 SEA ABB=ON PLU=ON L7 AND L8 AND L9  
L11 6 SEA ABB=ON PLU=ON L7 AND (L8 OR L9)  
L12 4 SEA ABB=ON PLU=ON L8 AND L9  
L13 4 SEA ABB=ON PLU=ON (L7 OR L8 OR L9) AND L6  
L14 11 SEA ABB=ON PLU=ON (L10 OR L11 OR L12 OR L13)

FILE 'REGISTRY' ENTERED AT 11:24:16 ON 20 AUG 2007

FILE 'REGISTRY' ENTERED AT 11:25:04 ON 20 AUG 2007

FILE 'BEILSTEIN' ENTERED AT 11:25:09 ON 20 AUG 2007

L15 0 SEA SSS SAM L3  
L16 10 SEA SSS FUL L3  
L17 6 SEA ABB=ON PLU=ON L16 AND BABSAN/FA  
L18 4 SEA ABB=ON PLU=ON L16 NOT L17  
SEL BABSAN L17

FILE 'BABS' ENTERED AT 11:26:05 ON 20 AUG 2007

L19 3 SEA ABB=ON PLU=ON (5574813/BABSAN OR 5503081/BABSAN OR  
5794913/BABSAN)

FILE 'ZCAPLUS, BABS' ENTERED AT 11:26:17 ON 20 AUG 2007

L20 18 DUP REM L6 L19 (2 DUPLICATES REMOVED)  
ANSWERS '1-17' FROM FILE ZCAPLUS  
ANSWER '18' FROM FILE BABS

FILE 'BEILSTEIN' ENTERED AT 11:26:52 ON 20 AUG 2007

FILE 'BABS' ENTERED AT 11:27:09 ON 20 AUG 2007

L21 1 SEA L20  
SEL BABSAN

FILE 'BEILSTEIN' ENTERED AT 11:27:30 ON 20 AUG 2007

L22 175 SEA ABB=ON PLU=ON 5574813/BABSAN  
L23 3 SEA ABB=ON PLU=ON L16 AND L22

FILE 'MARPAT' ENTERED AT 11:28:47 ON 20 AUG 2007

L24 2 SEA SSS SAM L3  
L25 31 SEA SSS FUL L3



L26 FILE 'ZCAPLUS, MARPAT' ENTERED AT 11:29:20 ON 20 AUG 2007  
 43 DUP REM L6 L25 (5 DUPLICATES REMOVED)  
 ANSWERS '1-17' FROM FILE ZCAPLUS  
 ANSWERS '18-43' FROM FILE MARPAT

FILE 'CAPLUS' ENTERED AT 11:29:37 ON 20 AUG 2007

L27 FILE 'HCAPLUS' ENTERED AT 11:29:41 ON 20 AUG 2007  
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 L28 3 SEA ABB=ON PLU=ON L27 AND (L7 OR L8 OR L9)  
 D COST

L29 FILE 'MARPAT' ENTERED AT 11:30:35 ON 20 AUG 2007  
 28 SEA ABB=ON PLU=ON L25 NOT (L7 OR L8 OR L9)  
 D COST FULL  
 L30 3 SEA ABB=ON PLU=ON L25 NOT L29

L31 FILE 'BABS' ENTERED AT 11:32:40 ON 20 AUG 2007  
 0 SEA ABB=ON PLU=ON (L7 OR L8 OR L9) AND L19

L32 FILE 'BEILSTEIN' ENTERED AT 11:33:18 ON 20 AUG 2007  
 0 SEA ABB=ON PLU=ON L17 AND (L7 OR L8 OR L9)  
 L33 0 SEA ABB=ON PLU=ON L18 AND (L7 OR L8 OR L9)  
 L34 4 SEA ABB=ON PLU=ON L18 AND RN/FA

L35 FILE 'REGISTRY' ENTERED AT 11:34:23 ON 20 AUG 2007  
 0 SEA ABB=ON PLU=ON L5 AND BEILSTEIN/LC NOT CAPLUS/LC

FILE 'REGISTRY' ENTERED AT 11:35:30 ON 20 AUG 2007

FILE 'ZCAPLUS' ENTERED AT 11:35:35 ON 20 AUG 2007  
 D STAT QUE L14

FILE 'MARPAT' ENTERED AT 11:35:50 ON 20 AUG 2007  
 D STAT QUE L30

FILE 'ZCAPLUS' ENTERED AT 11:36:58 ON 20 AUG 2007  
 D IBIB ABS HITSTR L14 1-11

FILE 'MARPAT' ENTERED AT 11:37:09 ON 20 AUG 2007  
 D IBIB ABS QHIT L30 1-3

FILE 'REGISTRY' ENTERED AT 11:37:47 ON 20 AUG 2007

L36 FILE 'ZCAPLUS' ENTERED AT 11:38:04 ON 20 AUG 2007  
 D STAT QUE L6  
 13 SEA ABB=ON PLU=ON L6 NOT L14

FILE 'BABS' ENTERED AT 11:38:21 ON 20 AUG 2007  
 D STAT QUE L19

FILE 'MARPAT' ENTERED AT 11:38:34 ON 20 AUG 2007  
 D STAT QUE L29

L37 FILE 'ZCAPLUS, MARPAT, BABS' ENTERED AT 11:39:11 ON 20 AUG 2007  
 40 DUP REM L36 L29 L19 (4 DUPLICATES REMOVED)  
 ANSWERS '1-13' FROM FILE ZCAPLUS  
 ANSWERS '14-39' FROM FILE MARPAT  
 ANSWER '40' FROM FILE BABS  
 D IBIB ABS HITSTR L37 1-13

D IALL L37 40  
D IBIB ABS QHIT L37 14-39

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 AUG 2007 HIGHEST RN 944998-48-5  
DICTIONARY FILE UPDATES: 19 AUG 2007 HIGHEST RN 944998-48-5

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<http://www.cas.org/support/stngen/stndoc/properties.html>

FILE ZCAPLUS

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FILE COVERS 1907 - 20 Aug 2007 VOL 147 ISS 9  
FILE LAST UPDATED: 19 Aug 2007 (20070819/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BEILSTEIN

FILE LAST UPDATED ON June 25, 2007

FILE COVERS 1771 TO 2007.

**FILE CONTAINS 10,004,722 SUBSTANCES**

>>>PLEASE NOTE: Reaction Data and substance data are stored in separate documents and can not be searched together in one query. Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a compounds with available reaction information by combining with PRE/FA, REA/FA or more generally

with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be searched as reaction partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

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\* **PATENT NUMBERS (PN) AND BABS ACCESSION NUMBERS (BABSAN) CAN NOW BE SEARCHED, SELECTED AND TRANSFERRED.**  
\* **NEW DISPLAY FORMATS ALLREF, ALLP AND BABSAN SHOW ALL REFERENCES, ALL PATENT REFERENCES, OR ALL BABS ACCESSION NUMBERS FOR A COMPOUND AT A GLANCE.**

FILE BABS

FILE LAST UPDATED: 25 JUN 2007 <20070625/UP>  
FILE COVERS 1980 TO DATE.

FILE MARPAT

FILE CONTENT: 1961-PRESENT VOL 147 ISS 7 (20070817/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	2007155779	05 JUL 2007
DE	102005063244	28 JUN 2007
EP	1801190	27 JUN 2007
JP	2007173472	05 JUL 2007
WO	2007076379	05 JUL 2007
GB	2433499	27 JUN 2007
FR	2895408	29 JUN 2007
RU	2302407	10 JUL 2007
CA	2571093	16 JUN 2007

Expanded G-group definition display now available.

FILE CAPLUS

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FILE COVERS 1907 - 20 Aug 2007 VOL 147 ISS 9  
FILE LAST UPDATED: 19 Aug 2007 (20070819/ED)